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VOL. X JANUARY, 1934 No. 1

Anniversary Discourse

MEDICINE AND MODERN SOCIOLOGICAL TRENDS

HON. JOSEPH V. MCKEE

My subject tonight, "Medicine and Modern Sociological Trends," has given me no little concern. When I accepted Dr. Sach's invitation to address your Academy on its 87th Anniversary and I had hit upon this as the title of my discourse, I did not realize my presumptiousness until I sat down to think of the subject to which I had assigned myself.

On one hand, my contacts with medicine have been rather casual, being no greater or no less perhaps than those of the average individual who prefers to witness the indignity of his physician wielding a niblick in a sand trap, to the frightening occultism of the same gentleman manipulating a fluoroscope in the darkened recess of his consulting room. And speaking objectively, even here my interest has been academic, for while I have scrutinized the expenditure of millions of dollars for medical services, a supersensitiveness has prevented the development, so to speak, of a bedside technique.

While I have often gone through the throes of early pneumonias, typhoids and anginas, especially after listening to physicians discuss the symptoms, I have never tarried at the sight of pain in others but have sought the solace of flight and the distraction of other things less disturbing. So, regarding the first part of my discourse, to ignorance I must add cowardice—two concepts that are of no great assistance to inspirational thought or profundity of reasoning.

Nor is my confidence restored when I turn to the second part—that of modern sociological trends. Because of the close relation of the sociological with the political, I must confess, in the words of the French, saying that "I know that I know not,"—a negative wisdom born of an experience of not too many weeks ago. However, from the more remote viewpoint of one deeply interested in human relations and the efforts of mankind for better social adjustments, I thought we might approach a consideration of these two topics in their interrelations, and from the humility of knowing not too much, point the way to some thoughts of benefit to minds busier with other things but, with all, deeply interested in the connotations of either or both of the subdivisions of our discourse.

To one who approaches the history of medicine from this viewpoint, there appears a phenomenon that recurs with surprising constancy down through the ages. This phenomenon lies in the interesting fact that the practice of medicine, more so than any other human endeavor, has moved onward under the impetus of influences outside the immediate field of medicine. In other words, it would seem to be that the great major movements in medicine have come, not from within medicine itself, but from influences outside of medicine but directly bearing upon it.

If this, my thesis, is correct, and I shall attempt tonight to give you examples of historical importance, then it is safe to assume that medicine today can be affected by those influences which are determinants of the social consciousness. Put it this way: If these influences were able to

modify the stream of medical thought in the first and the second and the third centuries, then it is a fair presumption that sociological influences can have their effect and will have their effect upon medical practice and principles of today.

With this in mind, it might be well to retrace our steps down through the corridor of the years and note, in passing, the influences, outside of medicine, that have been a tremendous factor in shaping medical achievement.

The first records of a rational or scientific medical system came from the Greeks. No nation has so excelled in pure reasoning as did the Greeks of Athenian and pre-Athenian glory. Yet, when we trace the beginnings of medicine, it was the influence of the people of Mesopotamia in their use of the entrails of animals in divination, who led the Greeks to the beginnings of a standardization of medical procedure. It was the influence, not of the Greeks, but of the submerged Minoaan civilization which gave us Aesculapius with his club and snakes, that led the way to the first ideas of sanitation and it was the Egyptians who pointed the way to the Greeks in the use of drugs and surgical instruments.

While the power of ratiocination was distinctly a flower of Greek achievement, it took the pragmatic influence of the people of Mesopotamia and Egypt to shape medical thought and practice so as to make possible the heritage of medical science to future ages. And yet, on the other hand, it was the philosophy of the Greeks which proved the impetus in the advancement of medicine, for medical science went forward with the culture of the Greeks and with the decline in that civilization, came the corresponding decline in the achievements of medicine. Hippocrates was the father of medicine but his influence was coterminus with the influence of Grecian philosophy and culture. It, therefore, is a safe premise that medicine was profoundly affected, not by medicine itself, but by those influences of thought and reason that made possible ing of a great intellectual age. It is interesting t while

Aristotle was not a physician, his power was tremendous in shaping medical thought for over two thousand years and while Galen's sway continued for thirteen centuries, it was an influence that brought no new great advancement in medical thought or science but was rather the force that bridged the centuries until the Greek influence should be reborn.

While thus we see medicine, in transmitting its Greek heritage, modified and shaped first by the empirical experience of a lower civilization and, secondly, raised to inductive and deductive reasoning by an age of philosophical ratiocination, so likewise, when we look at the story of medicine in the Roman republic, we find it again under the influence, not of philosophy, but of a military ideal which was a power tremendous in its immediate effect and incalculable in shaping the trends of later civilization.

Here was not the refining fires of a great philosophy that left in its ashes the residuum of a universal principle. Here a lower order, not that of pure reason, but of practicality, which gave an impetus that was local in its application and yet pointed to possibilities that took centuries to evaluate and develop. What would medicine have been without the influence of military exigencies? In the development of a definitive public medical service, the army that meant Rome did a service of inestimable benefit. Had it not been for the need of making the sick soldier well, the glory that was Caesar's might well have been satisfied with a sorry development of the Aesculapian Temple, the resort of the slave who in sickness sought the supplication of the Son of Apollo and Coronis and in obtaining his restoration in body, gained also his political freedom. Who can say what the story of medicine in the Roman Empire might have been were it not for the efforts of the army in building hospitals, in laying out great water works that gave the imperial city 300 million gallons of water a day, in raising standards of sanitation and establishing a medical service that saw to the appointment of physicians to towns and institutions?

In ancient Greece, it was the higher reasoning of philosophy; in Rome, the influence of an army that can fight only if it is well. And when these two great dynamic influences were dissipated in the dusk and shadows of the centuries preceding the Renaissance, we see the almost static condition of medicine that seemed content to follow for fourteen centuries the teachings of Galen whose theories were to be dissolved into nothingness in the crucible of a newly awakened consciousness. It is a striking thing and yet a natural one that with the decadence of thought in the middle ages, when men were content to distinguish, rather than to question, medicine likewise showed its greatest poverty and moved no higher than in the concentric circles of a dialectic age.

But with the rebirth of thought, with the coming of an age that questioned even the accepted fundamentals of a satisfied civilization, we see again the outward influence working its inward way upon medicine and medical thought.

The renewal of Greek culture, which in its essence was the study of pure reason, the invention of printing, the study of art which meant the study of anatomy, the recurrence of epidemics, but most of all the tendency to question—all these, beginning in the 16th century, were outside influences that were to give a new birth to medicine and to send it winging like a moth from a chrysalis of centuries to new and unheard of heights of accomplishment.

The work of Fracastro in syphilis and typhus, de Baillon in whooping cough and rheumatism, and Sydenham in gout and measles, was the result of the twin influences of a social demand to rid a people of the dread of communal afflictions and secondly of an age that discarded the dialectic philosophy of the cloister for the stimulating questions of the alembic and the retort.

An age that turned its inquisitive eyes to the results of experimentation in the physical sciences was soon to exert an inspiring influence on the study and practice of medicine and here again we see, both subjectively and objec-

tively, a great profession growing wider and deeper in its scientific attainments because of the work done in the sister sciences of physics and chemistry.

Who can tell adequately the modification of medical thought through the work of Harvey and Boyle? Whether or not medicine claims them as its own, there is no question that the age was such in its trend toward experimenting, in its breadth of vision and its ability to assume new bases of reasoning, as to provoke a profound effect upon the leaders of medicine and made possible the opening up of new paths that today are fundamental highways of medicine. In other words, without the influence of the age, what the result? In a negative sense no one knows. At least this is true, where the influence of original thinking was absent or a great social or economic or military force was lacking, when these conditions were not present, medicine showed inertia, contentedness and a history of the commonplace.

With the coming of the 18th century, we see a new influence under whose reaction medicine moved along new paths to greater service and efficiency. This time it was not philosophical or military or the result of activity in the allied sciences. It was a new force that was to gain in momentum until it reached down into the consciousness of communities, changed their viewpoints of responsibility and led to reforms in communal activities unheard of and undreamed of. It was the gospel of social justice; the publicizing of human rights, the realization of society's obligation to the individual—it was this new concept of government that had its great reflection in public health and with it the consequent raising of standards of sanitation in the cities and towns of England. The social concepts of Jeremy Bentham brought home to the law makers of England the obligation of society to insist upon higher standards in the management of those things that affect the common health. As a result, medicine, directly and collaterally, received a great impetus in fulfilling its mission
ly restoring to health but of preventing illness. It

was a new side of medicine that since has been carried to such standards of perfection and such control that death rates have been lowered many degrees and the average life added to by some ten to fifteen years.

What about our own time? Here again within the past generation we have seen great forces at work on medicine and medical practice, so strong as to subject it to important changes—changes that do not take the years to spell out but which he who runs can read.

Here we might call it a social-economic influence. It is that principle of action that took the shoe from the shoemaker and gave him a special part of it, that took the machine from the mechanic and gave him a wheel or a driving rod or a gear to work on; that took from the artisan the objective of creative genius and made him the perfecting unit in a scheme of which he was a part but did not dominate.

Speed, mass production, mechanical inventions, these have had a profound effect upon all human endeavor and in a marked degree upon medicine and medical practice.

Where has the general practitioner gone? And why? He has been replaced by the specialist and the specialist is here because the socio-economic influence that has been at work in other fields of human endeavor has affected the practice of medicine today. Who can gainsay the benefits? Who will not admit the faults and defects? These are subjects for discussion by those better trained than I. I point them out, however, to prove my point that even today medicine is reacting to these outside influences just as medicine was deeply affected by the philosophy of Aristotle, the intellectual unrest of the 16th century, the biochemical studies of the 17th and 18th and the economic and social changes of the 18th and 19th centuries.

And now today we stand at the threshold of a new era, an era limitless in its possibilities, an era fraught with great social and political changes. We are facing new con-

cepts in human relationships that in their development will go far to break down former principles of action, sweep away age-long convictions and substitute measures of public and government control undreamed of in any scheme of modern society.

This should not occasion too great surprise. The oak is a growth of roots, hidden perhaps, but no less strong because out of sight. The changes that are taking place in social relations seem new, perhaps, but the seeds have been planted for some years past and their roots given sustenance and strength by acts, perhaps unrelated in themselves. but all tending to assist in the growth of the full-blown tree.

No great social movements occur over night. They are the results of years of iteration, of attrition of the opposition, of constant but small and undetectable movements in one direction. Then, when ready, it is the dramatic incident, or perhaps accident, that brings their larger and more complete outlines to the public consciousness.

This sociological phenomenon of the ages, even though it may not be dramatically epitomized as in the granting of Magna Charta or the beheading of Louis XVI and Marie Antoinette or the battle of Concord or the slaying of the Archduke of Austria, has its counterpart in the deep-seated and fundamental changes already taken place in the American concept of the individual's rights and responsibilities and those of his government and in the radical changes that must flow in the future from measures already put into action.

The most clearly defined lines of this present-day social movement can be found in the cost of government. In the last twenty, and more so in the last ten years, billions of dollars have been added to the public debt. Not only has the cost of local municipal government risen by leaps and bounds but also that of state and the federal government. Nor is this increase limited to any one area of the country. So great are the financial obligations of our cities and

states that by far the greater percentage of American municipalities are bankrupt and with few exceptions the others are laboring and straining to avoid defaults. It will be only by the most extreme methods, if at all, that the federal government will be able to balance its budget. The consequent burdens of taxation are becoming still heavier with their crushing weight approaching the confiscatory.

Why? In anger and irritation we censure the politician and lay the blame on his door-step, charging him with waste, corruption and extravagance. But is this altogether true? I hold no brief for any of the conditions that result from political maladministration and here I might say, parenthetically, that the American people get pretty much the kind of government they want, or at least permit to continue. But, let me here point out that in the main, government is expensive, not because of the politician, but because of the changed social attitude of the American citizen in the conduct of his communal activities through governmental agencies.

Let me give you some examples. New York City pays out over $100,000,000 a year for education. What kind of education? The same education that the children of thirty and forty years ago received? Not at all. The simple red school house, with its benches and perhaps a map or a globe for equipment, has been superseded by a plant that costs over a million dollars which contains a swimming pool, a dental clinic, a gymnasium or two, full kitchen equipment for teaching cooking, a carpentry shop, a radio and a moving picture machine. When we leave the elementary school and go into the high school, particularly the so-called technical high school, we find there a unit of education that costs from 3½ to 4 million dollars, with courses that train the pupils for employment in many varied fields of human endeavor. Or we may find a class, with special equipment, and teachers for cardiacs or the crippled or the blind.

Expensive? Certainly. But not necessarily from extravagance. Rather these are the result of the modern conception of our social obligations. They are the results of

a public determination that government, whether local, state or federal, should take over new obligations that either were not recognized before or which were left for the individual to struggle with. Fifty years ago, society felt that bad teeth were no concern of education. They were the individual's problem and whether he overcame their handicap or not mattered nothing to any one but himself. So, too, with all the other activities now correlated with education and deemed an essential part of it but which have nothing to do with spelling or arithmetic or geography.

In other words, we have undergone a changed conception of the obligations of society. Not only do we continue for a much longer period the school in loco parentis but we have placed upon it new functions and duties that formerly, if they were performed at all, were carried on by the individual and at his own expense.

Nor has this new social concept been limited to the schools. The cost of public medical service, I exclude the free service of private institutions, has in the last twenty or thirty years doubled and trebled itself. Why? Because of extravagance? I should not say so. Rather this has come again from the insistence of the people themselves, not the politicians. Old services have been improved and extended and new services instituted. Public health service has long since left the narrow confines of caring in a left-handed way for the destitute sick but each year adds to the functions that precede even the individual's birth and extend beyond his death. Slowly, but surely, the government is assuming more and more the work of the private physician and holding forth to the patient opportunities for treatment that in former years could not be obtained or if they were available, only at the patient's own expense.

Let us go farther than the field of medicine to see further evidence of this new social concept. The care of the widow and her children by government agency is very recent in its origin. The very beginnings of this responsibility assumed by society occurred just previous to my ser-

vice in the State Legislature. Yet, in the intervening years, from 1918 to 1933, the cost of caring for the widow and the deserted mother, crept from something like a million dollars to over ten millions. Why? Extravagance of the politicians? No! It was a new social concept that made government responsible first for the widow and children of the citizen, then the deserted mother, then the wife of the imprisoned husband, an ever-widening circle of new obligations. I point to these as examples of an attitude of the mind of society—that government assume in ever increasing detail and expense not merely the education of the young or the care of the sick but also the care of the family.

It is only a few years ago that the legislature decreed that the community had a new responsibility—the care of the old. The old age security act was but another step in the direction I have been speaking of: the shifting of responsibility from the individual to the government. The allowance to old people in New York City last year reached the total of over 10 million dollars. A new sociological viewpoint decreed that this was an obligation that society had toward the aged individual and one which the collective agency of government must assume for the general welfare of human kind.

I could give you many instances of this new ideal—the inspection and regulation of factories, the limitation of the hours of labor by government decree, the conditions under which men and women could work, the taking over by the government of the responsibility to see that new standards of living and labor, both in tenement and factory were invoked—all these are indicative of the great movement that marks our time—all simple in their own fields and yet being parts of a great social movement uncomprehended until the units, as in a jigsaw puzzle, are joined together in a picture that startles by its completeness.

Gradually, but steadily, we have been adding the stones to the structure, until today, amazed by the necessities of an economic crisis, we see the structure we have builded.

In a winter of discontent, when a social and economic debacle has given us the disturbing and disquieting picture of over 10 million people out of work and in want, we begin to see how far we have gone down a road untrod before in the history of this country.

With this gradual change in our social and governmental concepts, it was most natural for men, whether bankers or business men, whether producers or middlemen or farmers, to look to the ultimate of this new social tendency—the government for the solution of society's pressing problems.

Responding to this new but very real influence, the banker accepted the domination of the government. He must insure his deposits; he cannot grant interest on his accounts; he must follow closely the dictates of a bureaucratic government that gladly assumes the obligations freely thrust upon it.

The business man, unconscious of the forces of government dependence, in the hour of fading profits and demoralization of trade, gladly accepts the standard imposed by government and agrees to a collectivism that would have been scorned and combatted ten years ago.

The farmer, beside himself with debt, looks to his government for aid and receives in return a premium not for the sowing and reaping of his harvests, but because he refrains from doing so.

The workman, out of work, yet seeking to save his family, not only from humiliation but also from starvation, obtains the aid of a government that appropriates three billion dollars for public works, useful in themselves, but made necessary by the hunger of ten million people who can obtain no succor except through this recourse to government.

What do all these things signify? Their significance lies in this, if anything: For the past twenty or thirty years, we have been extending the activities of government for the solution of our social problems. Little by little, we went

down this path but with a degree of progress that has been constant and far reaching.

Now, with this great economic crisis upon us, we have turned instinctively to the government for the solution of all our troubles—social and economic. We stand today, banker and broker, business man and farmer, producer and consumer, with our arms outstretched, to the great god of government, pleading, beseeching, imploring the use of its ever-extending power for the solution of all our ills. Like the downfall of Louis XVI, we realize a revolution is upon us—not that of the serf seeking relief from the feudal lord, or the peasant of France from the salt tax or the people of America from a stupid and arrogant England, but a socially-minded nation seeking the ultimate of what has been projected as a final goal when first the tiniest obligations were shifted from the individual to the shoulders of the collected people, through the agency called government.

I am not, nor shall I be, argumentative. I am not discussing the relative merits or demerits of this new regime of society. I neither approve nor disapprove. These are questions for debate by others. I am simply trying tonight to be factual and from the facts to point not only to the road down which we have traveled but along which we must trace our steps in the immediate years to come.

If this is the modern sociological trend—to look more and more to the government for the solution of our social, our economic and our business problems, what will be the effect upon medicine and medical practice, that has shown a tendency to be most responsive to the great influences of every age, whether it be Greek or Roman, English or American?

As I see it, this new collectivism means a portentious thing for medicine. Medicine in the laboratory is one thing and perhaps as far as sociology is concerned, less subject to influences other than those of science and experimental achievement. But as far as medicine has its counterpart in communal activities, then can we expect it to be subject to

those new influences which dictate the common good and give more and more authority to government for the fulfillment of its concept of that ideal.

Will a science, so close to the common welfare and touched with this ideal of communal service, remain free from the influences that have modified education, labor, business and productive activities generally? The answer is apparent. The influence is there and strong. Will it bring about a socialization of medicine? Will men trained in medicine and surgery become agents of a super-developed state that decrees the highest standards of public health and promotes health service?

Does the future of medicine lie in being merely an agency of a government that assumes responsibility for all health conditions? In this new but gradual collectivism, where will medicine takes its stand? These are questions that are not idle. These are questions, the answers to which will affect the future of medicine as strongly and fundamentally as did the reasoning of Des Cartes or the discovery of Harvey or the specialization of the Rockefeller Institute.

It is not for us to draw a cloak over our eyes and say that this is not so or to decry conditions that already exist. For good or evil, they do exist. In the development of our civilization, these influences today are showing effects that no one who thinks can deny.

What then are we to do? It is idle to speak of the old days, which we would fain characterize as good. They have passed and it would seem forever. The appropriation of three billion dollars for unemployment or the call for the spending of millions for new services for the poor sick, the widowed and the aged, is not to be measured in money values but in the new ideal on which they are founded. We are in an era that is the result of a new concept of the obligations of society as translated into action by government.

As I see it, it is for medicine to recognize a new day in social relationship and rather than be driven to new ideals of service, to accept the leadership which should naturally

flow to it because of the great men and women who dominate its work and its destiny. Rather, I would see medicine, which down through the centuries, has been moved by outside forces and influences, assume a new leadership—not merely that of the laboratory or the clinic, the bedside or the hospital, but a leadership in thought and ideal in those fields that secondarily affect medicine and by that leadership, make medicine the protagonist of a new and great era, rather than the maid servant of those, who leading in other sociological fields, by secondary influence shape the destiny of medical practice.

If present conditions do not meet with our approval, if these tendencies are not to our liking, is it not foolish for us to withdraw to the sidelines and point the finger of scorn or disapproval? Rather, it is for those who believe in the highest ideals of medicine to participate all the more actively, not merely in medicine but in those other fields of sociology and economics and politics so that medicine may not only be a handmaiden of a civilized age but also a great factor and influence in the advancement of those things that tend properly and fundamentally toward the ultimate happiness of mankind.

The Hippocratic oath speaks of an ideal for the physician: "I will look," it says, "upon him who shall have taught me this Art as one of my parents. I will share my substance with him and I will supply him necessities if he is in need. . . . The regime I adopt shall be for the benefits of my patients according to my ability and judgment and not for their hurt and for any wrong."

This is the dedication, the consecration of the physician to the ideals of his profession. But more than that is asked of him today. With these great sociological movements under way and even at fruition, it calls on him not merely to complain, not merely to disagree, not merely to debate but to find a fuller and a freer and a greater place for medicine, not only in the curing of human ills but in the great regime to make life better and happier and nobler—to bring to humankind some of the happiness on earth that the elect expect of heaven.

ANNUAL GRADUATE FORTNIGHT
"DISORDERS OF METABOLISM"
October 23 to November 3, 1933

THE METABOLISM OF FEVER*

With Special Reference to Diabetic Hyperpyrexia

HAROLD E. HIMWICH
Yale University School of Medicine

It is a great honor to be invited to address you this evening, an honor I especially appreciate because it permits me to be on the same platform with my teacher and friend, Dr. Eugene F. DuBois. Since I am essentially a laboratory worker, your committee evidently believes that the study of medicine is advanced by laboratory experimentation as well as by observation at the bedside. Tonight, I hope to present a point of view on fever gained solely in the laboratory. The clinician will be able to test this work by bedside observation, and to modify the conception in the light of his own experience.

A description of fever may well begin with a discussion of the mechanisms for the regulation of the temperature of the body. What maintains the normal temperature at a relatively constant level? An analysis of this question reveals that certain processes tend to raise the temperature of the body, while others have the opposite effect. Most of the physiological activities of the body are attended by the production of heat; muscular exercise, for example, or the digestion of food. Indeed, the body would soon attain a temperature incompatible with life were it not for mechanisms which make for the dissipation of heat. There are two important means by which heat loss occurs. One is by radiation and conduction from the skin which is normally warmer than the environment and therefore loses heat. The other mechanism is the evaporation of water in

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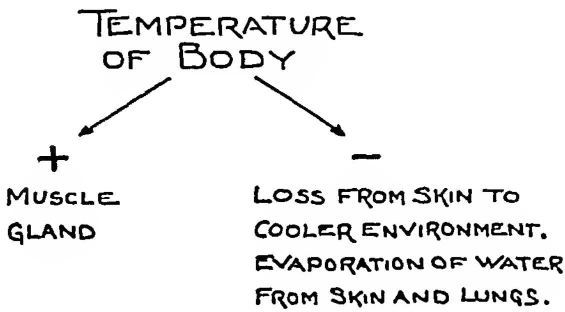
* Delivered October 23, 1933.

the form of perspiration from the skin and moisture from the lungs by which process heat is also dissipated from the body.



Thus, in the healthy individual, these two opposing groups of mechanisms balance each other in such fashion that the temperature remains close to 98.6° F. or 37° C. I say "close" to 98.6° because it is commonly known that there exists a diurnal variation in the temperature of the body of approximately 1.5° F., the temperature being highest in the afternoon and lowest about 12 hours later in the morning. However, except for this diurnal variation, under most normal conditions the body temperature remains remarkably constant so that marked deviations from 98.6° must be construed either as a temporarily uncompensated physiological process or as a frankly pathological change. Such a deviation indicates that the balance between heat production and heat loss has been altered. Traube (1863) in the latter half of the 19th century attempted to show that fever in every case is due to one factor only, namely, inadequate loss of heat. Traube's conception is correct only in so far that in all fevers heat loss is obviously inadequate. If the heat dissipating mechanisms eliminate sufficient heat there can be no fever. However, Traube is wrong when he says that disturbance of the mechanisms of heat loss is the only factor. In certain fevers, notably those of infectious or toxic origin, there is another very important element—the increased production of body heat. A classical study which revealed these points was made by Dr. DuBois

Classification of Fevers

(1) With normal mechanisms for the production and elimination of heat the elimination cannot cope with the formation of heat either because the production is too rapid as in diathermy and in extreme hyperthyroidism or because of an environment too hot and humid to permit adequate loss of heat, as in sunstroke.

(2) In most infectious diseases there is a pathological conservation of heat. Heat production is increased but the elimination processes do not act as in the healthy individual for despite the greater heat production, the body acts to conserve heat. The arterioles to the skin close as though the body had been thrust into a cold bath and the cutaneous blood supply diminishes (Fremont-Smith, Morrison, Makepeace, 1929). In this manner a lesser amount of heat is lost to the environment and accordingly the body temperature rises.

(3) There is another group of fevers in which heat loss is pathologically reduced. This group of fevers is associated with anhydremia. In anhydremia the volume of the blood is diminished, particularly due to loss of water. The small amount of blood remaining in the body is employed to supply the vital organs. As a result, there is not a sufficient volume of blood to spare the usual quota for the periphery of the body. The skin becomes relatively cold and the loss of heat to the environment diminishes. Thus, even with an unchanged production of heat, the body temperature rises.

Anhydremia has been produced in infants by increasing the food intake and at the same time limiting the ingestion of fluids. Finkelstein (1908) has shown that increased carbohydrate or salt in the dietary of infants may produce fever. Bakwin (1922) has demonstrated that the inanition fever of newborn babes is associated with an increased concentration of blood serum indicating a diminution of the water content of the blood and of the body. With the administration of fluids both the concen-

tration and the temperature returned to normal. Woodyatt and his co-workers (1919) adduced striking evidence that the injection of hypertonic glucose with the resulting tremendous polyuria and consequent dehydration produces a grave hyperpyrexia. This pyrexia was cured by increasing the water content of the injected solution. Similarly, the polyuria of the diabetic patient is a potential cause of anhydremia and hyperpyrexia. Lande (1933) recently analyzed a series of cases from Mt. Sinai Hospital and called attention to the clinical importance of diabetic hyperpyrexia. He believes that this syndrome may be due, among other causes, to anhydremia.

III.

Since the term "fever" embraces such a variety of conditions, the remainder of the discussion will be confined to an experimental analysis of diabetic hyperpyrexia, which has been carried on in the Laboratory of Physiology at Yale during the last few months with the cooperation of Mr. Fazikas. The observations were made on dogs rendered completely diabetic by the previous surgical removal of the pancreas. After the pancreatectomy the animals were maintained on a diet of meat and sugar to which pancreatin was added. Insulin was injected twice daily.* When the dogs had remained in a satisfactory condition from one to two weeks, they were considered fit for experimental study.

The next step consisted in the production of the diabetic hyperpyrexia. One of the outstanding features of diabetes consists in alterations of water metabolism as indicated by the symptoms of polydipsia and polyuria. Since water occupies such an important position in the heat regulating mechanisms of the body it at once suggested itself that the polyuria of diabetes might play an important role in

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* The insulin was generously supplied by Eli Lilly and Company through the courtesy of H. W. Rhodehamel, Director of Research.

the pathogenesis of diabetic hyperpyrexia. In order to imitate this polyuria which for our purposes consists chiefly of a loss of water and salt it was necessary simply to withhold insulin from the depancreatized dogs. The high blood sugar following this procedure produced a polyuria, a loss of fluids from the body. To accentuate and intensify the loss of fluids not only insulin but also water was withheld from the diabetic animals.

You may well imagine our pleasure when this simple technique resulted in the production of marked fever in our experimental animals. Indeed, it was possible to produce fever of more than 104° F. with striking ease and regularity and it is the functional pathology and clinical features of this fever which I desire to present to your attention this evening.

That the simple procedure of withholding insulin and water reduces the volume of the circulating blood can be seen in the following table. Here it will be observed that the specific gravity of the blood serum rose from 1.0251 to 1.0309 during a period of three days, while the temperature rose from 100.9 to 105.3.

TEMPERATURE AND SPECIFIC GRAVITY DURING DIABETIC HYPERPYREXIA

Water Intake	Temp. °F	Specific Gravity of Serum
Ad. Lib.	100.9	1.0251
None for 9 hours...........	102.2	1.0277
None for 24 hours..........	105.3	1.0309

The great increase in the specific gravity of the serum determined by the method of Barbour and Hamilton (1926) indicates that the water content of the blood has been correspondingly diminished—that there is an anhydremia. The specific gravity is an indicator of the amount of solids in the blood. As solids increase there is a proportional decrease in the water content. Certainly, in this experiment the anhydremia increased along with the tem-

perature. That there is an anhydremia during diabetic acidosis is well known (Chang, Harrop and Schaub, 1927-28, Peters, Kydd, and Eisenman, 1933).

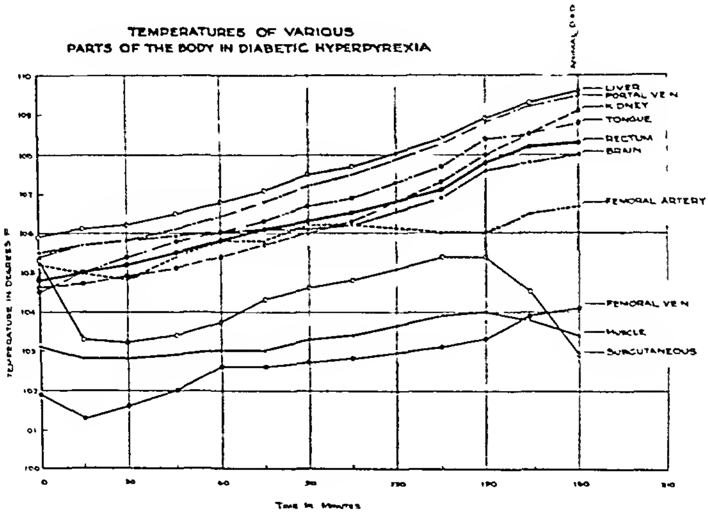
Anhydremia During Diabetic Hyperpyrexia

Water Intake	Temp. °F	Sp. Gravity	Osmotic Pressure	Oxygen Capacity Vol. %
Ad. Lib.	102.4	1.0245	0.894	20.04
Ad. Lib.	99.5			
None for 30 hours	104.2	1.0315	1.149	24.83

In these observations on dog No. 10 the specific gravity increased from 1.0245 to 1.0315. The evidence for dehydration is striking but to strengthen this point further confirmation was attempted by other methods. When water is abstracted from the blood stream there may be a relative retention of salts if the salts do not leave the blood as rapidly as does the water. Since the osmotic pressure of the serum is due largely to the salts the osmotic pressure should increase with the concentration of the salts.

In this experiment the values for the osmotic pressure of the serum were determined according to the procedure of A. V. Hill (1930) by Dr. Gilman of the Department of Pharmacology. You see that the osmotic pressure rises with the increase of body temperature. As water leaves the blood the red blood cells remain and that increases the number of the red blood cells per unit volume of blood. Since the hemoglobin of the red blood cells carries oxygen, a greater oxygen capacity of the blood indicates that the relative amount of red blood cells has increased. You will note a great rise in the oxygen capacity of the blood at the height of the fever. Thus, the results of the measurements of specific gravity, osmotic pressure and oxygen capacity exhibit a perfect harmony in indicating an anhydremia. There is, therefore, a parallelism between the development of the anhydremia and the rise of the temperature of the body. This suggests that the diminution of the water reserves of the body is the causative factor of the fever exhibited by these animals.

In passing, I should like to point out that along with this increase in the specific gravity of the serum, there must be a greater viscosity of the blood. With a greater concentration of solids the blood will meet with more resistance as it passes through the vessels. The bearing of this finding on our problem will be dealt with later in this discussion.



Another characteristic of the syndrome of anhydremic hyperpyrexia is the relationship between the temperature of the mouth and the internal organs of the body to that of the skin and musculature. With Dr. Greenburg of the Department of Public Health measurements were made of the temperature of various parts of the body by means of thermocouples. Previous workers had found the liver the warmest part of the body and in anhydremic fever the same relations obtain. The various internal organs, brain, kidney, portal vein, are not very different in temperature from that of the rectum or mouth. As the rectal temperature increases all those viscera suffer a rise in temperature. The temperature of the arterial blood is somewhat lower than that of the rectum as has been observed by Wright and Johnson (1933), for the temperature of the arterial fluid is influenced by that of all parts of the body. In addition to the warm blood coming from the various viscera

there is the colder blood of the femoral vein draining the lower extremities.

In the graph, presenting the observations on an untreated diabetic animal, dog No. 3, you will note the divergence of the temperature of muscle and subcutaneous tissue just beneath the skin from that of the other organs. The muscles of the extremities and the skin form a separate group in which the temperature does not as a rule rise. These experiments indicate that the blood is kept away from the skin which otherwise would be warmer. Presently, evidence will be presented for the belief that the mechanism producing the relatively bloodless skin is that of a reflex closure of its vessels, *i. e.,* the nervous system sends impulses to the cutaneous vessels causing them to constrict. However, at this time it is sufficient to make the point that, due to the relatively cold skin, little heat is lost via that route. In a word, the fever is caused chiefly by the fact that the skin is losing an inadequate amount of heat to the environment.

The temperature usually existing in the muscles of the extremities during fever like that of the skin is in marked contrast with that of the internal organs. It is, therefore, highly probable that these muscles are relatively anemic, perhaps also as a result of the reflex closure of the arterioles. Marriott (1920) has observed that the blood flow in the extremities of anhydremic infants may be reduced from one-fifth to one-tenth that of healthy infants. Whatever the exact mechanism may be which limits the blood supply of the muscles it is therefore interesting to determine the effects of the diminished blood flow. A diminished blood flow to any organ means a reduction of its oxygen supply. In muscle inadequate oxidation is followed by the accumulation of lactic acid which finally pours into the blood stream. Therefore, if the oxygen afforded the muscles is insufficient for their needs, analyses of the blood should reveal an accumulation of lactic acid. Returning to the

observation of dog No. 10 it will be seen that lactic acid in the blood rises along with the fever.

CHANGES DURING DEVELOPMENT OF DIABETIC HYPERPYREXIA

Water Intake	Temp. °F.	Lactic Acid mg. %	pH	Alkaline Reserve Vol. % Whole Blood	Acetone Substance mg. %
Ad. Lib.	102.4	25	7.38	40.13	
Ad. Lib.	99.5				
None for 30 hours	104.2	45	7.25	32.40	2.5

LACTIC ACID OF URINE
Mg: per 24 Hours

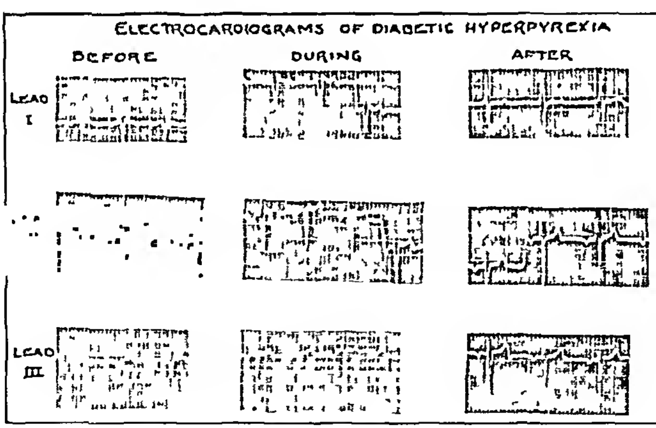
	Bisulfite Binding During Fever	Substances After Fever	Lactic Acid Excess During Fever
Dog No. 15.........	1131	180	1151
Dog No. 16.........	1929	114	1885

In 1924, Starr and Fitz noted the presence of an unknown organic acid in the urine of patients with diabetes. This unknown acid which was not comprised in the group of acetone substances was present in the urine of 10 per cent of their patients. Our observations reveal that the unknown organic acid is none other than lactic acid, for a portion of the lactic acid accumulated in the blood is excreted by the kidneys. The table discloses the increase of the lactic acid content of the urine during diabetic hyperpyrexia. In the calculation of urinary lactic acid, the bisulfite binding substances determined according to the technique of Friedemann, Cotonio and Shaffer (1927), were estimated both at the height of fever and after defer-

vescence. The excess of bisulfite binding substances occurring during fever was reckoned as lactic acid as in the work of Hewlett, Barnett and Lewis (1926-27).

It is of importance to determine the effects of lactic acid in the blood on the acid-base equilibria. The pH of the blood measured by Delafield DuBois (1932) exhibited a decrease indicating the development of an acidosis. The alkaline reserve of the blood is also diminished by the presence of lactic acid. The acid-base equilibria of the blood may be influenced by many factors, for example, the inorganic acids and bases. Determination of the total base and chloride of the serum revealed that the changes in the alkaline reserve of the whole blood may be attributed to those of lactic acid. Gesell (1918-19) noted a decrease of the alkaline reserve during the anhydremia of hemorrhage.

IV.



Since voluntary muscle exhibits evidences in diabetes of an insufficient supply of oxygen, it becomes of special interest to determine how the most important muscle of the body—namely, the heart, acts under these conditions of anhydremic hyperpyrexia. Here you see three series of

electrocardiograms of dog No. 10 taken by Dr. Nahum. The first series shows the control after pancreatectomy, before anhydremia was developed. You will note that the tracing of the S-T segment is in its usual position on the isoelectric line. The next series shows an electrocardiogram taken during an anhydremic fever of 104.2°. Here the tracing of the S-T segment shows a shift to a position well above that of the isoelectric line. The usual significance of such a change is insufficient oxygenation of the heart itself. Ischemia of the heart may occur in any condition in which the cardiac musculature receives an insufficient supply of oxygen, for example in arteriosclerosis, coronary thrombosis or asphyxia. The mechanism which produces this change is a matter of conjecture. Since the heart is one of the vital organs of the body it is difficult to believe that a reflex to its coronary vessels would be employed to limit the blood flow, though such might possibly be the case. Perhaps the great increase in the viscosity of the blood might be a factor, for with an increased viscosity the blood may pass through the smaller vessels so slowly as to make it impossible to deliver an adequate amount of oxygen in a given time. It is not likely to be due to a greatly diminished blood pressure since the animal showed no indication of shock. On the contrary, it was lively and jumped out of its cage. Without further studies, we cannot be sure of the mechanism of causation. However, in any case, the changes in the electrocardiogram are identical with those occurring during oxygen lack of the heart—a functional asphyxia. These changes of the electrocardiogram are not the result of the increased temperature *per se*, but of the anhydremia. Nevertheless, it is not impossible that alterations in the heart other than those of asphyxia may have a similar effect on the electrocardiogram. It is significant, however, that electrocardiograms of anhydremic children taken by McCulloch (1920) revealed the same changes of the S-T segment.

Let us now see the complete picture. As a result of dehydration due to withholding of fluids and to polyuria in a diabetic animal, there is a diminution of blood volume

V.

Decreased Blood Volume or Anhydremia	Decrease in Blood Supply to Skin → Hyperpyrexia
	Decrease in Blood Supply to Muscle → Lactic Acid
	Changes in E.K.G. similar to those of insufficient oxygen supply to heart

and of body fluids. Evidence of this is found in the increased specific gravity, osmotic pressure and oxygen capacity of the blood. Due to the diminished water content of the body, a characteristic syndrome develops in which may be included changes of temperature, lactic acid and of the heart. The temperature of the vital organs does not fall; on the contrary, it rises because of insufficient heat loss through the skin and lungs. There is not a sufficient volume of blood for circulation through the skin which, therefore, becomes relatively cold. As a result of the diminished output of heat from the skin, hyperpyrexia develops, because of the inadequate supply of blood to muscle the oxygen afforded is insufficient and lactic acid accumulates. The electrocardiogram also yields evidence which may be interpreted as indicating oxygen lack in the heart.

VI.

If the picture of diabetic hyperpyrexia just drawn be a true one and the proposed explanation be correct, the successful application of one single test should serve to confirm it. The administration of water should restore all the changes characteristic of this syndrome to their original status, and at the time preserve the life of the animal. This, in fact, has been achieved by intravenous injection and oral ingestion of fluids, and it has been found possible to save life by initiating these simple procedures, even at a body temperature of 105.5° F.

CHANGES DURING DEVELOPMENT AND REGRESSION OF DIABETIC HYPERPYREXIA

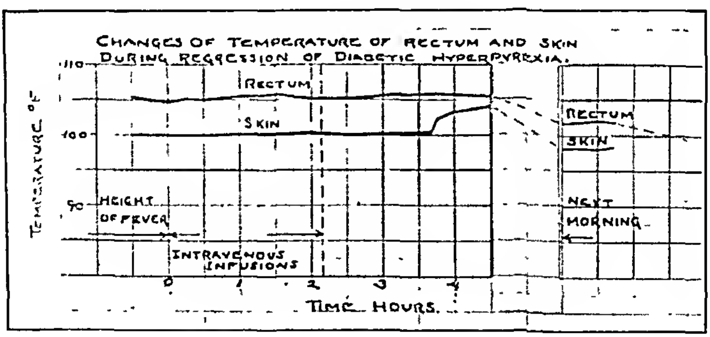
Water Intake	Temp. °F	Sp. Gravity	Osmotic Pressure	Oxygen Capacity Vol. %
Ad. Lib.	102.4	1.0245	0.894	20.04
None for 30 hours..	104.2	1.0315	1.149	24.83
700 c.c. in 3 hours..	102.2	1.0254	1.099	20.69
1000 c.c. in 10 hours	100.4	1.0246	1.016	19.58
Ad. Lib. for 26 hours	99.5	1.0234	0.876	19.74

The first part of these data you have seen before. It was presented to show some of the blood changes during the development of the diabetic hyperpyrexia. When the temperature attained the value of 104.2° F. fluids were administered by mouth and insulin was injected subcutaneously. In approximately four hours the body temperature had fallen almost 4° F. Very striking is the agreement between the rise and fall of the temperature and the changes in the water content of the blood. The changes in specific gravity, osmotic pressure, and oxygen capacity all show first, a great diminution in the water content of the blood and during the cure a reversal to normal values. The specific gravity falls from 1.0315 at the height of the fever to 1.0234; the osmotic pressure from 1.149 to 00.876 and the oxygen capacity from 24.83 vol. per cent to 19.74 vol. per cent. There can be no doubt of the close correlation between the water content of the blood and the temperature of the diabetic animal.

CHANGES DURING DEVELOPMENT AND REGRESSION OF DIABETIC HYPERPYREXIA

Water Intake	Temp. °F	Lactic Acid mg. %	pH	Alkaline Reserve Vol. % Whole Blood	Acetone Substance mg. %
Ad. Lib.	102.4	25	7.38	40.13	
None for 15 hours..	104.2	45	7.25	32.40	2.5
1150 c.c. for 30 hours	102.2	70	7.18	32.32	0
1000 c.c. for 10 hours	100.8	16	7.29	37.92	4.2
Ad. Lib. 26 hours...	99.5	17	7.35	37.99	

The other changes in the blood exhibit a similar advance and regression. Twenty-five mg. per cent of lactic acid is somewhat high for a normal value. Forty-five mg. per cent is one that is definitely increased. The rise to 70 mg. per cent may well be attributed to the washing out of the lactic acid accumulated in muscle once the normal blood flow had been reestablished. Finally, lactic acid returns to a normal value. The pH is affected by the concentration of lactic acid and the pH of the blood indicates that an acidosis developed with the accumulation of lactic acid, and decreased when the lactic acid was removed. The changes in the alkaline reserve are also largely determined by those of lactic acid. As the lactic acid content of the blood rose from 25 mg. per cent to 45 mg. per cent the alkaline reserve diminished from 40.13 to 32.40 vols. per cent. The further increase of lactic acid to 70 mg. per cent was followed by no greater fall of the alkaline reserve probably because the fluids administered at this time contained base in the form both of chloride and bicarbonate. Again the acetone substances do not appear to affect the alkaline reserve to a noticeable degree.



The temperature of the various parts of the body, especially of the rectum and skin exhibit an interesting series of changes. Here are the results obtained on dog No. 3 in which treatment was instituted after the temperature had mounted to 105.5°. At this point the animal was put under

amytal anaesthesia and one thermocouple was inserted in the rectum and another placed on the skin. These registered automatically and you will note that the skin temperature was approximately 100° and the rectum 105.5°. After the initial readings had been made fluids were administered intravenously. One liter was given during a period of approximately 2 hours. For more than 1½ hours following the infusion there was no marked change either in the skin temperature or in the rectal temperature. Then suddenly the skin temperature began to rise, as if the arterioles of the skin had opened, and had permitted more blood to enter the cutaneous area. The skin temperature rose almost to 104.0° F. and the rectal temperature nevertheless remained the same for some time longer. The next morning, however, both skin and rectal temperature had diminished. Sufficient heat had been lost by the skin to reduce the skin temperature to 98.5° F. and that of the rectum to 101.5° F. At this time the animal recovered from the amytal anaesthesia; therefore, the succeeding observations were made with a mercury thermometer until the rectal temperature fell to 99.5° F. Thus the rectal temperature decreased only after heat was lost by the skin. In other words, the body must bring blood to the periphery to lose heat. If you recall the temperature relations while the fever was advancing you will remember that the skin decreased in temperature as the rectal temperature rose. There is, therefore, an inverse ratio between skin and rectal temperature. The skin temperature decreases as the rectal approaches a maximum while in recovery from fever the skin temperature rises before the rectal temperature is able to fall. The fact that in the experiment on dog No. 3 the skin temperature did not change for some time after the intravenous infusion of fluids had been administered would indicate that the arterioles to the skin were shut at first and did not permit blood to enter the cutaneous vessels. Such an action would lend evidence for the point of view that the skin was kept in its relatively bloodless condition as a result of a reflex closure of its smaller vessels which later were relaxed only some time after the

fluid content of the body had been increased. We believe that the same mechanism obtains in the musculature of the extremities since the muscles, like the skin, are also relatively cold during the development of the fever. At this time we do not wish to commit ourselves as to the mechanism causing the changes in the heart. However, it is of great interest and importance to note that these changes of the electrocardiogram also regress with the administration of fluids. The effect of a fever of 104.2° in the S-T segment may be seen in the figure. Within 48 hours of the ingestion of fluids there is a marked change—the S-T segment is lowered to the isoelectric line, and in 24 hours the electrocardiogram is indistinguishable from the original control.

It has thus been possible to trace the regression of all the changes attendant upon the development of diabetic hyperpyrexia simply as a result of the ingestion of fluids. This affords striking evidence for the belief that lack of water is the prime factor in the production of this syndrome.

VII.

It is obviously of some importance to make a similar study of diabetic hyperpyrexia in human patients. Suggestive is the work of Hartmann and Darrow (1928) who noted an increased concentration of lactic acid in the blood of some of their patients. I am not aware of any observations made with the electrocardiograph.

It is not always practical to make the various laboratory tests necessary for the demonstration of anhydremia. Of great aid in establishing the diagnosis, however, is a history of polyuria, vomiting and limited fluid intake. These are suggestive of anhydremia in a patient with diabetes and fever. Moreover, the patient may exhibit such definite signs of anhydremia as those of dry tissues and soft eye balls. It is of some advantage to know that the anhydremia is roughly proportional to the fever. Until the fever subsides the water content of the tissues may be considered inadequate. If no other cause for the fever can be found, then the extent of the fever may be taken as an indication of the degree of anhydremia.

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PROCEEDINGS OF ACADEMY MEETINGS

DECEMBER

STATED MEETINGS

Thursday Evening, December 7

ORDER

I. Executive Session at 8:30 o'clock

a. Reading of the Minutes

b. Election of Academy Officers

c. Election of Fellows and Members

II. The Anniversary Discourse at 8:45 o'clock

"Medicine and modern sociological trends," Hon. Joseph V. McKee.

Thursday Evening, December 14, at 8:30 o'clock

The Third Harvey Lecture, "Heteroplastic Grafting in Embryology," Professor Ross G. Harrison, Sterling Professor Biology, Yale University.

This lecture takes the place of the second Stated Meeting of the Academy for December.

SECTION MEETINGS

Joint Meeting

Section of Surgery and the Section of Medicine

Friday Evening, December 1, at 8:30 o'clock

I. Reading of the Minutes

II. Presentation of Cases

a. Thyrocardiac disturbances—2 cases, Arthur S. McQuillan

b. Thyrocardiac disturbances—2 cases, Emil Goetsch

III. Papers of the Evening

a. The medical treatment of the thyrocardiac, Cary Eggleston

b. The operative treatment of the thyrocardiac, William Barclay Parsons

IV. General Discussion

Malcolm Goodridge, Stuart Hart, Richard Lewisohn, Morris K. Smith

Section of Dermatology and Syphilology

Tuesday Evening, December 5, at 8:30 o'clock

ORDER

I. Presentation of Cases from New York University and Bellevue Hospital Medical College

II. Presentation of Miscellaneous Cases

III. Discussion of Selected Cases

Section of Neurology and Psychiatry

Tuesday Evening, December 12, at 8:30 o'clock

ORDER

I. Reading of the Minutes

II. Papers of the Evening

a. Delinquency problems in a children's court, Helen Montague (by invitation)

b. Evaluation of classification in prisons, J. L. McCartney, Elmira (by invitation)

c. Modern treatment of crime, V. C. Branham, Albany

III. Discussion

Bernard Sachs, Judge Jonah B. Goldstein (by invitation), Menas S. Gregory, Henrietta Additon, Deputy Commissioner (by invitation), Bernard Glueck (by invitation)

IV. Executive Session

Section of Pediatrics

Thursday Evening, December 14, at 8:30 o'clock

ORDER

I. Papers of the Evening

a. Serum phosphatase as a criterion of the severity and of the rate of healing of rickets, Aaron Bodansky (by invitation), Henry L. Jaffe (Hospital for Joint Diseases)

b. Serum protein deficiency without reversal of the albumin: globulin ratio, A. A. Weech (by invitation) (Babies' Hospital)

c. Studies in measles prophylaxis, Bela Schick, Samuel Karelitz (Mount Sinai Hospital)

d. Variations in serum bases of infants and children in disease, Aubrey B. MacLean, Ruth C. Sullivan (by invitation) (St. Vincent's Hospital)

e. Studies in amyloidosis, Harold G. Grayzel (by invitation), Mendel Jacobi, Hyman Warshall (by invitation), Maxwell Bogin (by invitation), Herman Bolker (by invitation), Benjamin Kramer (The Jewish Hospital of Brooklyn)

Section of Orthopedic Surgery

Friday Evening, December 15, at 8:30 o'clock

ORDER

I. Reading of the Minutes

II. Presentation of Cases

a. Correction of equinus deformity of os calcis in congenital club foot, Leo Mayer

b. Demonstration of Schultze osteoclast for correction of congenital club foot, Nicholas Ransohoff

c. Cases showing early and complete correction of equinus in congenital club foot, John C. McCauley, Jr. (by invitation)

III. Paper of the Evening

Treatment of congenital club foot, J. H. Kite, Decatur, Georgia (by invitation)

IV. Discussion

Percy W. Roberts, John J. Nutt, Isadore Zadek, Arthur Krida

JOINT MEETING

Section of Medicine and the Section of Ophthalmology

Tuesday Evening, December 19, at 8:30 o'clock

ORDER

I. Reading of the Minutes

II. Papers of the Evening

a. The ocular complications found in the study of 2000 diabetic patients (Dr. Joslin's patients), J. Herbert Waite, Boston (by invitation)

b. The ocular complications of diabetes, Russell M. Wilder, Mayo Clinic (by invitation)

III. General Discussion

Elliott P. Joslin, Boston (by invitation), John Wheeler, Arthur J. Bedell, Albany, Bernard Samuels

Special Notice

Section of Ophthalmology

Monday Evening, December 18, at 7 o'clock

Instruction Hour was carried on as usual: External Diseases—Symptomology, Pathology and Treatment, Dr. Algernon B. Reese

Section of Obstetrics and Gynecology

Program arranged by the Obstetrical Staff of the Knickerbocker Hospital

Tuesday Evening, December 19, at 8:30 o'clock

ORDER

I. Reading of the Minutes

II. Presentation of Cases

a. Puerperal Parotitis—2 cases, Mortimer W. Rodgers

b. Siamese Twins—caesarian section—hysterectomy, George G. Bemis (by invitation)
Discussion—Leon T. LeWald, George L. Brodhead, Arthur Stein

c. Placenta Acreta, Edwin G. Langrock
Discussion—Locke L. Mackenzie, Meyer R. Robinson

d. Spontaneous rupture at the cervico-vaginal junction during labor at term, Ralph L. Barrett (by invitation)
Discussion—Samuel J. Scadron, Edwin W. Holladay, George L. Brodhead, Arthur Stein

III. Paper of the Evening

A statistical study of six years' work in the Maternity Service at the Knickerbocker Hospital (lantern slides), George L. Brodhead, R. H. Shrady (by invitation)

Discussion—Edwin W. Holladay, George L. Brodhead

Section of Otolaryngology

Wednesday Evening, December 20, at 8:30 o'clock

ORDER

I. Reading of the Minutes

II. Presentation of Cases

a. Osteomyelitis of the skull following acute sinus infection, with intracranial complications, Hampton P. Howell (by invitation), Howard A. Patterson

b. Two cases of osteomyelitis of the skull following sinusitis and orbital cellulitis, C. C. Wolcott (by invitation)

III. Papers of the Evening

a. The regression theory of otosclerosis, Louis K. Guggenheim, St. Louis (by invitation)
Discussion opened by Arthur B. Duel, Edmund P. Fowler

b. Osteomyelitis of the skull, A. C. Furstenburg, University of Michigan (by invitation)
Discussion opened by Ira Cohen, Robert E. Buckley, Rudolph Kramer, Harmon Smith

Section of Genito-Urinary Surgery

Wednesday Evening, December 20, at 8:30 o'clock

ORDER

I. Reading of the Minutes

II. Papers of the Evening

a. Some of the neglected affections and lesions of the deep urethra in the male, Edgar G. Ballenger, Atlanta, Georgia (by invitation)
Discussion opened by Howard S. Jeck.

NEW YORK ROENTGEN SOCIETY

in affiliation with

THE NEW YORK ACADEMY OF MEDICINE

Monday Evening, December 18, at 8:00 o'clock

I. 8:00 to 8:30 p. m.
Demonstration and discussion of interesting cases

II. 8:30 p. m.
Clinical Meeting. Members demonstrated films of cases in which the diagnoses have been proved by operation, autopsy or therapeutic response.

New York Meeting of the

SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE

under the auspices of

THE NEW YORK ACADEMY OF MEDICINE

Wednesday Evening, December 20, at 8:15 o'clock

I. Experimental evidence of an additional substance essential to mammalian nutrition, L. N. Ellis; introduced by H. C. Sherman

II. Clinical use of prolactin, R. Kurzrok, R. W. Bates, O. Riddle, E. G. Miller

III. Effect of barbiturates in experimental nephrosis, W. S. Murphy, T. Koppanyi

IV. Metabolism of various sulfur compounds in cystinuria, E. Brand, G. F. Cahill, M. M. Harris

V. Reaction of transplantable and spontaneous tumors to blood-carried bacterial toxins in animals unsusceptible to Schwartzman phenomenon, F. Duran-Reynals, introduced by J. B. Murphy

VI. A contribution to the etiology of encephalitis. Differentiation of encephalitis by protection test, L. T. Webster, G. L. Fite

VII. Experimental poliomyelitis. Active immunization with neutralized mixtures of virus and serum, S. D. Kramer, M. Schaeffer, introduced by A. J. Goldforb

VIII. On the motility of the colon of the dog, T. S. Raiford, M. G. Mulinos

NEW YORK PATHOLOGICAL SOCIETY

in affilition with

THE NEW YORK ACADEMY OF MEDICINE

Thursday Evening, December 28, at 8:30 o'clock

ORDER

I. Demonstration of Pathological Specimens

II. Papers of the Evening

a. Blood groups and therapeutic malaria, Silik H. Polayes, Irving M. Derby (by invitation)
b. A case of non-lipoid histiocytosis, with necropsy, Nathan Chandler Foot, Charles M. Olcott
c. The histopathology of Paget's disease, Vera D. Dolgopol
d. The pigmented mole as a tactile organ; its place in the evolution of hair follicles, George F. Laidlaw, Margaret R. Murray (by invitation)

RECENT ACCESSIONS TO THE LIBRARY

Bigelow, G. H. & Lombard, H. L. Cancer and other chronic diseases in Massachusetts.
Boston, Houghton, 1933, 355 p.

Burnet, É. Prophylaxie de la tuberculose; applications en Europe.
Paris, Masson, 1933, 375 p.

Clendening, L. Behind the doctor
N. Y., Knopf, 1933, 458 p.

Cottet, J. Les troubles de l'élimination urinaire de l'eau.
Paris, Masson, 1933, 211 p.

Dietlen, H. Die Lungentuberkulose; eine Einführung in ihre Entstehung, ihre Entwicklung und ihre Verlaufsarten.
Dresden, Steinkopff, 1934 [1933], 142 p.

Földes, E. A new approach to dietetic therapy.
Boston, Badger, [1933], 434 p.

FELLOWS AND MEMBERS ELECTED DECEMBER 7, 1933

For Fellowship:

Edward A. Atwood	360 Park Avenue, Paterson, N. J.
Theodore Neustaedter	27 East 93 Street
E Gordon Stoloff	1085 Park Avenue
George Thomas Pack	155 East 72 Street
Harold Abramson	1097 Madison Avenue
Nicholas J Poltchaninoff	35 Nathan Davis Place
William Clifford Ivins	214 East Hanover Street, Trenton, N. J.
William Beverly White	65 South Street, Stamford, Conn.

For Membership:

Alfred A. Schwartz	7 West 71 Street

For Associates:

Robert Morris Fischer, D D S	73 East 90 Street
Jerome M Schweitzer, D D.S	643 West 246 Street
Marjorie T Bellows, A B	9 Greenridge Avenue, White Plains

ALFRED FABIAN HESS

The Council of The New York Academy of Medicine expresses its profound sorrow over the death of its distinguished member, Dr. Alfred Fabian Hess.

His work has been of such signal importance in the development of American medicine, that the Academy is proud to have had among its members a man who has left behind him the reputation of having been not only a great physician, a distinguished pediatrist, an original investigator, but one who may truly be called a benefactor of mankind.

During his brief career he has earned the gratitude of the medical world, both here and abroad. As President of the Harvey Society, his leadership was characterized by an unusual devotion to, and respect for, pure and exact science. The resolutions passed by the Harvey Society include so fine a summary of his achievements, that the

Academy is ready to adopt these resolutions as an expression of its own sentiments regarding Dr. Alfred Fabian Hess.

BERNARD SACHS, *President.*

The Harvey Society learns with profound regret of the death of the distinguished President of the Society, Alfred Fabian Hess. In the lengthening list of its Presidents, none has been more devoted to its interests, none has sought more earnestly to maintain its fame, none has devoted more energy to the realization of its purposes. He exhibited his sympathetic attitude by consenting to return to a former custom of the Society to occupy his office for two successive terms. In the second of these, unexpectedly and in the full tide of his powers, his grievous loss is sustained. He has been a member since 1911 and has himself been one of its lecturers (Jan. 15, 1921).

Doctor Hess has numerous claims to the high regard of his professional colleagues. Beyond the custom of most men, his life was given solely to the interests of his calling. He knew no divided allegiance; the whole of his thought and energy exhibited extraordinary singleness of purpose. A life of contented leisure, so easily within his choice, he exchanged by preference for one of laborious days. These he consecrated to the furtherance of useful knowledge and this he placed unreservedly at the disposal of his fellow men. Two books and 225 separate contributions to journals are witness to this choice and serve as his fitting memorial.

His researches fall into two categories. There is an earlier one in which his activities were dominated by the prevailing interest in communicable diseases. His thought took, as it usually did, two directions, one social, one scientific. Problems connected with the spread of tuberculosis engaged his attention first. In the Laboratories of the Department of Health in this city he studied "The Incidence of Tubercle Bacilli in New York City Milk" (1909), an investigation which led to important recommendations for the protection, especially of infants, from infected milk. The concern which he entertained for the welfare of chil-

dren led him to suggest a plan for the institutional treatment of infants exposed to this scourge. To this end he developed the idea of "A Tuberculosis Preventorium for Infants" (1917) which led then to the realization of a Preventorium for Infants at Farmingdale (N. J.). At this period he was interested also in certain phases of other communicable diseases. In writing on "A Protective Therapy for Mumps" (1915) he discerned in the method he was proposing a solution not merely of special importance but one—and this was eminently characteristic of the penetrating quality of his reflective nature—involving a general principle, applicable to the treatment of measles and since then tested in relation to other comparable diseases.

Although he retained his interest in communicable diseases, he soon turned, at the Laboratories of the Board of Health and later in the Home for Hebrew Children and the laboratories of the College of Physicians and Surgeons at Columbia University to his studies on scurvy and on rickets. Investigations on these subjects he continued to pursue with unflagging energy throughout his life. It was this field to which his main and outstanding contributions to knowledge were made. At the time of his death he was engaged in analyzing no less than six separate aspects of these problems. How extraordinarily fruitful these researches were, it is perhaps too early completely to appreciate. In number alone, their wealth bears witness to his very great industry. But meritorious in itself, industry alone would not have achieved for him his well earned fame. In more than one direction he broke new paths. The subject is so well known as to require no extended description—the relation of scurvy and rickets to the vitamins, the influence of sunlight and the seasons on the progress of the disease rickets, the importance in its treatment, of artificial light, of various foods, and of various oils, the development of non-potent into potent agents when exposed to ultra-violet rays. In these researches his prime endeavor was to extend knowledge, but his critical intelligence was content with nothing less than that pitfalls due to too early

generalization should be avoided; anti-rachitic agents he saw were not of equal value, for they exhibit differences depending on their origin and on their utilization. And in this case as in that of tuberculosis he did not lose sight of the wider prophylactic uses to which his investigations could be put; he saw to it that the general public benefitted by making practical underlying theoretical considerations.

The method by which he carried on his activities is not the least of the interesting phenomena which distinguish the ways of this gifted man. Having entertained an idea —and he had many—he tested it, first rationally, with the utmost meticulousness. He defined it carefully in words so that by observation and experiment he was in position to know precisely what it was which he wished to subject to exact analysis. Having analyzed it, he was not content unless an experiment, which to him was never more than an analogue, was genuinely illustrative of a clinical situation. If he found a solution to an initial question, he proceeded to further development or elaboration of the plan originally entertained. It was an impressive intellectual process, slow and careful procedure from step to step, which those who knew him came to appreciate and which those who knew him less intimately did not in the end escape from recognizing.

How devoted he was to the acquisition of knowledge, quite apart from its meaning for his personal career, can be discerned from a further study of his technique. His investigations forced upon him the need to rely upon methods, both chemical and physical, with which his own education and later training, had not prepared him. From the challenge of their use he did not shrink. In principle, and for his purposes, he developed a sure acquaintance with their significance. But from a personal technical utilization of them he had the good judgment to refrain. His disinterestedness in the pursuit of knowledge and his generosity in sharing his ideas are exhibited with singular clearness when he found himself in this situation. It was then that he turned to other men, suitably equipped, to

come to his aid. His insight into problems connected with the physics and chemistry of the vitamins was in fact unusually penetrating. His prophetic vision on more than one occasion forced upon reluctant associates enthusiasm sufficient to embark on researches which, without his stimulation, would not then have been undertaken. It is a general judgment that the organic chemistry of this group of substances is richer as a result of the interest which he aroused and to which he turned as the result of his clinical experience. He knew his limitations, but he knew also how to surmount them. He not only cultivated a field but he shared its cultivation with his fellows.

This description of a singular man would be incomplete if other aspects of his personality were left unmentioned. Aside from his industry, aside from his scientific insight, aside from his inventiveness, he had an unusual historical sense. Were this side of his interests not known otherwise, it would emerge from reading those chapters in his book on rickets in which he describes the history of this disease. He cared not only for knowledge of the development of ideas in regard to it, but he charged himself with the collection of the literature of this subject and has by his collection made the Library of the New York Academy of Medicine the richer. Those who were privileged to sit with him on the Committee of that Library were aware of his sensitiveness to the meaning of the march of ideas in the development of conceptions.

He was conscious also of another obligation. As a scientific man, he made the interests of scientific men his personal concern. In this city in which social intercourse among like-minded men is difficult, he made of his home a center of hospitality, a center for the discussion and exchange of ideas. That the discussions were uniformly elevated and of a high seriousness, the character of the man amply assured.

Wherever on the numerous sides of interest appropriate to the lives of medical men one looks, the death of Alfred Hess marks loss. He touched life in many of its phases; wherever he touched it, he enriched it. Without the oppor-

tunity for disciples, his intellectual vigor, his disinterestedness, his pungent personality impressed itself upon his contemporaries.

The Harvey Society is conscious of its loss. To his associates, to his friends, to his family, it expresses its deep sympathy.

JAMES W. JOBLING
WILLIAM H. PARK
ALFRED E. COHN, *Chairman*

The following resolution upon the death of Dr. Alfred F. Hess was passed by the Committee on Library at a meeting held January 9, 1934:

The Committee on Library of The New York Academy of Medicine possessed in Doctor Alfred Fabian Hess a friend to the Library and an associate in the guidance of its activities whose comradeship they greatly valued. As a member of the Committee from 1928 to 1932, and Chairman in the last of these years, Dr. Hess' interest in the Library was constant and productive. He strengthened it as an institution and gave generously to it from his store of wisdom and of books.

The Committee wish to express to Mrs. Hess their sense of personal loss in the death of Dr. Hess.

ELI MOSCHCOWITZ,
Secretary of Committee on Library

DEATHS OF FELLOWS AND ASSOCIATE FELLOW OF THE ACADEMY

CHAPMAN, CHARLES FRANCIS, M.D., Mount Kisco, New York; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1890; elected a Fellow of the Academy January 4, 1906; died, December 26, 1933. Dr. Chapman was a Fellow of the American Medical Association and a member of the County and State Medical Societies. He was Surgeon to Northern Westchester Hospital, Mount Kisco, and President of the Westchester County Medical Society.

Franken, Sigmund Walter Anthony, D.D.S., 151 Central Park West, New York City; graduated in dentistry from the New York College of Dentistry in 1909; elected an Associate Fellow of the Academy March 3, 1927; died, December 13, 1933. Dr. Franken was a member of the First District Dental Society, The New York State Dental Society, The American Dental Association, The Association for the Study of Internal Secretions, and the New York Academy of Science. Since 1920 he has been Chief of the Dental Clinic at Lenox Hill Hospital in New York City.

Moschcowitz, Alexis Victor, B.A., Ph.D., M.D., 925 Madison Avenue, New York City; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1891; elected a Fellow of the Academy April 5, 1900; died, December 21, 1933. Dr. Moschcowitz was a Fellow of the American Medical Association, a Fellow of the American College of Surgeons, a member of the County and State Medical Societies, the American Surgical Association, the American Association for Thoracic Surgery, the International Surgical Association, the New York Surgical Society, the Alumni Association of Lenox Hill Hospital and the Pathological Society. He was Professor of Clinical Surgery in the College of Physicians and Surgeons, Columbia University. He was Consulting Surgeon to Mount Sinai, Israel-Zion, Bronx Maternity and Woman's Hospitals. Dr. Moschcowitz served the Academy in many ways. At the time of his death he was a member of the Committee on Fellowship.

Williams, Linsly Rudd, B.A., M.A., M.D., 130 East 67 Street, New York City; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1899; elected a Fellow of the Academy May 5, 1904; died, January 8, 1934. Dr. Williams was a Fellow of the American Medical Association, a member of the County and State Medical Societies and the American Public Health Association. He was Director of the National Tuberculosis Association from 1922 to 1928. He became Director of The New York Academy of Medicine in January, 1924, and President of the New York Tuberculosis and Health Association in February, 1928, and held these offices at the time of his death. He occupied many other important positions in connection with public health and the advancement of medical practice.

BULLETIN OF
THE NEW YORK
ACADEMY OF MEDICINE

VOL. X | FEBRUARY, 1934 | No. 2

LINSLY RUDD WILLIAMS

The Council at its regular meeting on January 24 voted to hold a memorial service to Dr. Williams in Hosack Hall at a date to be announced later, the arrangements for which are to be placed in the hands of a special committee.

It is planned that the speakers at this meeting will represent the various activities of Dr. Williams' many-sided life.

The Council further voted that a special volume shall be published by the Academy as a memorial to Dr. Williams in which will appear the resolutions adopted by the Council, the various Committees of the Academy and other organizations, the addresses delivered at the memorial service, and other contributions.

ANNUAL GRADUATE FORTNIGHT
"DISORDERS OF METABOLISM"
October 23 to November 3, 1933

METABOLISM IN HYPERTHYROIDISM AND HYPOTHYROIDISM*

WALTER WALKER PALMER

A comprehensive review of the field of metabolism in diseases of the thyroid gland is obviously an impossible task in the brief space at our disposal, nor would it serve the purpose for which these gatherings are designed. During the past two decades the interest of the physiologists and physicians in the subject has resulted in numerous investigations which have brought forth now well established facts of great value to the practitioner. The purpose of this talk is to consider some of the practical problems in the diagnosis and management of diseases of the thyroid in so far as alterations in metabolism are concerned.

By far the most common diseases of the thyroid are believed to be due to either diminished or increased activity of the gland, in its elaboration and discharge into the general circulation of the hormone thyroglobulin. Of the thyroid insufficiencies, myxedema in adults and cretinism in children are easily recognized clinically. The diffuse symmetrical enlargements of the thyroid gland at puberty and in the low iodine areas are associated with a slight insufficiency. All conditions in which there is over-activity are usually designated as hyperthyroidism, "toxic thyroids" or exophthalmic goiter. Fortunately malignant disease of the thyroid is much less common as is also acute and chronic thyroiditis.

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* Delivered October 24, 1933.

Basal Metabolism

The level of the basal metabolism is now recognized by both physiologists and clinicians as one of the best indications of the activity of the thyroid gland. As early as 1893 Friedrich Müller called attention to the emaciation and loss of weight in spite of the high caloric intake in exophthalmic goiter patients which suggested to him that the total metabolism was increased in this disease. By 1897 Magnus-Levy had demonstrated an increased oxygen consumption in hyperthyroidism, and diminished oxygen consumption in cretinism and myxedema. It was not until 1912 that the work at the Russell Sage Institute of Pathology and Carnegie Nutrition Laboratory provided us with an apparatus and method for the determination of basal metabolism which was suitable for clinical purposes. Since then the apparatus has been simplified and improved so that at the present time basal metabolism determinations have become a part of the routine in all well organized clinics and many doctors' offices. As a test of thyroid activity basal metabolism determinations have proved of great value in diagnosis and treatment of the diseases of the thyroid gland. There are, however, certain limitations of a laboratory test of this type. The technic, while not particularly difficult, is full of pitfalls which may lead to errors amounting to 10 or even 20 per cent. The normal standards in general use are for most purposes adequate, but it should be remembered that an occasional normal individual may have a basal metabolism well outside the range set as normal for the test. The diet and state of nutrition are important. In the under nourished the metabolism is lower while in the well nourished it may be elevated. The state of mind, the trained versus the untrained subject, the muscular tone are all factors necessary of consideration in slight or moderate variations from the normal mean. While there may be a tendency for errors in different directions to neutralize one another there is always a possibility of a co[illegible]ation tending to a large discrepancy in a single inst[illegible] [illegible]rtain diseas[illegible]

there are well recognized variations from normal. A slightly elevated metabolism is frequently found in hypertension, malignancy, pregnancy, acromegaly, leukemias, polycythemia and infections. On the other hand, a lowered basal metabolism may be present in the anemias, Addison's disease, many skin diseases, tumors of the pituitary gland and in diabetes.

Thyroid Insufficiencies

The physician receives little help in identifying myxedema or cretinism from basal metabolism determinations. The clinical picture is characteristic and unmistakable. The B.M.R. is usually 30 per cent or more below the normal average. A B.M.R. of —40 per cent is considered to indicate a total lack of thyroid activity although as low as —59 per cent has been reported. Supplying the needed hormone by the administration of one of the several thyroid preparations can be successfully and safely carried out if reasonable care be exercised. A certain comfort, however, is derived from following the effect of treatment with basal metabolic rates. Inconsistencies between the clinical picture and the B.M.R. do occur as the following case will illustrate. An unmarried woman of 35 presented a classical picture of myxedema. Repeated B.M.R. determinations were within normal limits, the lowest value being —11 per cent. Subsequent experience revealed the fact that with six grains daily of the Burroughs Wellcome preparation all signs and symptoms of myxedema disappeared although the B.M.R. never went above +6 per cent, except on one occasion when the patient on her own account increased the daily intake to eight grains. After two weeks she developed outspoken symptoms of hyperthyroidism, nervousness, sweating, and a rapid pulse. Her basal at this time was +19 per cent.

Situations more confusing and difficult are those met in patients with a low B.M.R. without the clinical features of myxedema. Some of these patients unquestionably have a diminished thyroid activity and are markedly improved

following the administration of thyroid substance sufficient to bring their B.M.R. to within the normal range. Others either have a low B.M.R. normally or are suffering from disturbances other than within the thyroid gland. The administration of thyroid gland as a therapeutic test is probably the best method of differentiating these cases. In addition to the effect on the clinical condition the B.M.R. control is of great advantage. Thyroid gland should be given in amounts sufficient to bring the B.M.R. to within normal limits. Occasionally the result is spectacular and improvement is striking. In other cases without any change in the B.M.R. the patient may complain of accentuation of existing symptoms and no clinical benefit result. Still others with large doses of thyroid extract no beneficial change is observed in the clinical picture nor is there the expected rise in B.M.R. Carefully controlled administration of thyroxin by mouth or parenterally may be tried. The low B.M.R. in our experience is encountered most frequently among those patients who complain of nervousness, easy fatigueability, sensitivity to cold and menstrual disorders. They are usually individuals who are worried over their ability to maintain a satisfactory social or economic position in the community; lack force of character; have a low blood pressure; and are poor physical specimens. As a rule their B.M.R. is seldom lower than —20 per cent and it is in this group that thyroid gland therapy is most disappointing. A small percentage of patients apparently exhibit what seems to be a true hypothyroidism, the B.M.R. is usually as low as —25 per cent or lower and they improve with thyroid gland administration.

The adolescent goiter is associated probably with slight insufficiency. Frequently the girls have a B.M.R. between —15 and —20 per cent. The normal variation of the B.M.R. among youths of the adolescent age is greater than among adults, frequently on the low side. Most of the individuals with adolescent goiter living outside the endemic goiter areas probably need little treatment. It is our practice, however, following the advice of Marine, to administer

August	26, 1930	+51	100	Sod. iodide increased to 0.2 daily.
September	3, 1930	+94	108	Good clinical improvement. Sod.
September	4, 1930	+84	92	iodide discontinued. Lugol's 2 mils daily.
September	9, 1930	+40	108	Partial thyroidectomy September 10, 1930.
September	18, 1930	+22	100	Made an excellent convalescence from operation.
September	22, 1930	+26	80	Discharged from hospital.
February	27, 1931			Gained weight and doing housework. Not nervous, no palpitation or tremor.
August	21, 1931	+65	76	No evidence of hyperthyroidism.
November	21, 1931	+68	88	No symptoms of hyperthyroidism.
August	19, 1932	+46	72	No discoverable enlargement of remnant of thyroid gland.
August	4, 1933	+40	68	Continued in excellent condition.

Were it not for the consistency of the several B.M.R. determinations, the accuracy of the observation might be challenged. There is a striking lack of correspondence between the B.M.R. and clinical condition. This case further illustrates the occasional lack of correlation between the pulse rate and B.M.R.

Heart Disease

Since the introduction of basal metabolism determinations into clinical use a real advance has been made in bringing to light cases of hyperthyroidism masquerading as heart disease. The test has served to improve the keenness of the clinical eye. Many of the patients in this category have few or no discoverable signs of hyperthyroidism and appear to be suffering solely from heart disease. The patient is usually over forty, frequently fibrillating, with unmistakable evidence of cardiac failure. There is no exophthalmos, no enlargement of the thyroid gland, no nervousness, profuse perspiration or tremor yet the B.M.R. may be markedly elevated. Attention may be drawn to these cases by the poor response to digitalization. Following partial thyroidectomy the clinical improvement leaves no doubt as to the correctness of the diagnosis.

Furthermore the pathological laboratory demonstrates a hyperactive gland on microscopic examination. As an illustration of this condition the following case is reported. L.B. (358799), 47, single woman, in domestic service entered the hospital October 20, 1932, complaining of dyspnea, palpitation, nervousness and insomnia. Her palms were not moist, there was no exophthalmos; the thyroid gland was moderately enlarged; the heart was enlarged with unmistakable signs of mitral stenosis, the rate was rapid and totally irregular. The diagnosis was rheumatic heart disease, mitral stenosis and fibrillation, with a debatable element of hyperthyroidism since she had an enlarged thyroid and a B.M.R. of +25 per cent. Several weeks of rest with digitalis resulted in no marked improvement. A partial thyroidectomy was performed following which the cardiac situation improved rapidly. Six months after operation there were no cardiac symptoms although she was still fibrillating without pulse deficit.

Another case—L.C. (367468), a Chinaman of 57 entered the hospital January 1, 1933, complaining of swollen legs, palpitation, dyspnea and cough with occasionally blood streaked sputum of three months' duration. He was an apathetic individual distinctly icteric, not suggesting hyperthyroidism in the least. The thyroid gland was slightly enlarged and possibly a slight stare noted in the eyes but no exophthalmos. His heart was large, without organic valvular disease, rate rapid and regular: His liver enlarged and tender: Edema of the lower legs. He was considered to be a case of arteriosclerotic heart disease. On rest and digitalis for several weeks no significant improvement was made. A basal metabolism determination was made and found to be +52 per cent. Partial thyroidectomy was followed by slow but distinct improvement, the jaundice cleared and signs of cardiac decompensation disappeared. He left for China April 10.

The extraordinary benefit derived from partial thyroidectomy in patients similar to these just described has led Blumgart and Levine to reduce the level of metabolism in

individuals with chronic heart disease but without hyperthyroidism by total ablation of the thyroid gland. Several cases are reported and the results give much promise. The period of observation has been too short to permit any definite statement concerning the advisability of so revolutionary a procedure.

One of the difficult problems with which the physician is frequently confronted is the differential diagnosis between psychoneurosis and hyperthyroidism. In many psychoneurotics the clinical picture is suggestive of hyperthyroidism. There may be a B.M.R. of +15 to +20 per cent. Each patient presents a particular situation and I know of no scheme by which a separation can be made with certainty. Without doubt many individuals have lost part of their thyroid gland unnecessarily and probably others have missed the opportunity of relief by operation. A large number of patients assigned to the group of psychoneurotics have normal B.M.R. so that any marked increase in basal should be viewed with suspicion. When doubt exists the patient with moderately increased basal should be closely observed in good circumstances, with rest and sedatives and frequent B.M.R.s made to determine its persistence. In certain of these cases the effect of iodine on the basal is of considerable diagnostic aid. If the B.M.R. be lowered following the administration of iodine then iodine should be discontinued to determine whether the basal is to return to its original level. A repetition of the experiment is desirable. A drop in the B.M.R. with clinical improvement following iodine administration is certainly suggestive of hyperthyroidism. On the other hand when no reduction of the basal is observed in such a procedure we consider the evidence in favor of the absence of hyperthyroidism.

Malignant Disease and Thyroiditis

The basal metabolic rate is of little aid in the diagnosis of malignant disease of the thyroid. Of twenty-four cases reviewed at the Presbyterian Hospital there were B.M.R.

determined on twelve. In eight cases the basal was within normal limits, the remaining —17 and —23 per cent, +39 and +80 per cent. The same may be said of acute and chronic thyroiditis. All of the basals in the few cases we have observed, eight in all, have been within normal limits.

General Metabolic Considerations

The effect of hyperthyroidism or hypothyroidism on the protein, carbohydrate and fat metabolism can be explained largely, if not wholly, on the basis of the increased or decreased level of heat production. With adequate fat and carbohydrate, protein minima correspond to those found in normals. There appears to be no difficulty in the utilization of carbohydrate on the part of the hyperthyroid and the inability to store it is due to the increased demand for food. It has been observed that the cholesterol in the blood is increased in hypothyroidism and decreased in hyperthyroidism. This fact is considered by Hurxthal of value as a differential diagnostic aid in puzzling cases but I have had no personal experience with it.

The enormous increase in heat production in hyperthyroidism means that an increased amount of food is needed for the patient. We hear the "high caloric diet" mentioned frequently in connection with the treatment of hyperthyroidism either surgically or medically. Many times the so-called high caloric diet as prescribed is inadequate. Numerous observations now confirm the fact that these patients require much more than the normal 10 or 20 per cent increase over basal requirements at rest. As much as 75 or 100 per cent increase over their basals may be necessary to maintain nitrogen equilibrium and bring about a gain in weight in the hyperthyroid patient. From a practical standpoint gain in weight answers the question whether the patient is receiving sufficient food. We have found the B.M.R. a useful guide in securing adequate food intake. It is usually possible by employing concentrated foods to get the patients to take twice as many calories as the B.M.R. calls for.

The role of iodine in the physiology of the thyroid is a fascinating topic but only a few practical phases of the subject can be mentioned. The place this element holds in the prevention of non-toxic hyperplasia of the thyroid gland and its value in preparation of toxic cases for operation is well established. The extent to which iodine reduces the B.M.R. is usually in direct proportion to the initial elevation. In 185 unselected cases we have studied at the Presbyterian Hospital the average drop in the basal after iodine administration when the level was between +20 and +30 per cent was 9 per cent; with an initial basal between +70 and +80 per cent the average drop amounts to between 35 and 40 per cent. The above observation served as a standard with which to compare the effect of diiodotyrosine which has been so enthusiastically recommended in the recent German literature as superior to the inorganic preparation in common use. Chemically diiodotyrosine would seem to be the precursor of thyroxin, moreover almost all of the organic iodine in the thyroid gland is in the form of either thyroxin or diiodotyrosine. On the hypothetical basis that these two organic iodine compounds normally are in equilibrium in the gland, hyperthyroidism might result when thyroxin is present in excess, hypothyroidism when diiodotyrosine predominates. Our chemical studies of normal and pathological glands have failed to bring support to such a hypothesis. The claims made for the therapeutic use of diiodotyrosine is that it reduces experimental hyperthyroidism, known to be unaffected by inorganic iodine compounds; that it is effective in so-called iodine refractory cases; and that iodine escape is less frequent. In a study of thirty cases including three patients who had previously received iodine, we could detect no difference in the effect of diiodotyrosine and that observed with Lugol's solution and sodium iodide. The reducing effect on the basals was commensurate in both preparations, nor was any change produced by diiodotyrosine in the iodine refractory patients. Our clinical experience with diiodotyrosine appears to be consistent with observations made in the laboratory. When rabbits are given gram

doses of diiodotyrosine about 10 per cent is excreted as inorganic iodine, the rest either unchanged or as a lactic acid derivative. When given in the therapeutic amounts of 100 milligram doses to patients a larger percentage may be broken down to give inorganic iodine.

A word of warning against the indiscriminate use of iodine may be ventured. We have already mentioned its use in the adolescent goiter and as a therapeutic aid in selected cases. Long continued use of iodine in patients with nodular glands occasionally transforms a non-toxic gland to a toxic gland. I know of no advantage to be gained in administering iodine to individuals with non-toxic nodular glands. The great value of iodine in bringing about remissions in the toxic glands, either diffuse or nodular, in preparation for operation must always be considered when one contemplates the use of iodine therapeutically in toxic cases. The temporary effect of iodine makes it essential to reserve iodine for pre-operative use. It is true that cases are reported, and I have seen such, demonstrating a control of the toxicity over long periods until spontaneous recovery occurs, but in my experience iodine has proved disappointing in the medical management of toxic goiter. The impression that once the iodine effect is obtained and the patient "escaped", little benefit may be expected in the subsequent use of iodine is not correct. After a period, one to four weeks, without iodine even though it has been administered over a several months' period we note satisfactory responses. It must be said, however, that the second trial often results in a less striking response.

Conclusion

I have endeavored to point out in the foregoing remarks how a knowledge of the deviations from normal of the metabolism in hyper- and hypo-thyroidism may be of service to the clinician. One impression I hope to make. Laboratory tests of function are valuable aids when given their proper place and importance. They have increased

our knowledge of disease and have contributed to our clinical ability. It must be remembered, however, that they often represent single components of a complicated system of dependent variables. The danger not only in diseases of the thyroid, but in Medicine generally, is to become a slave to laboratory data and place too little reliance on good clinical judgment.

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SURGICAL TREATMENT OF HYPERTHYROIDISM*

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It is my desire and purpose to present to you informally the results of our experiences with hyperthyroidism in its typical, in its atypical form and in its association with other diseases.

First I would like to speak about the question of hyperthyroidism in children.

We have seen now a large number of children ranging down to as young as three years of age with typical exophthalmic goitre. At the beginning of our experience with hyperthyroidism, particularly in very young children, we were greatly worried by this condition because of the great capacity of children to react so strikingly to intoxications of any variety. We were impressed, almost intimidated, by the tremendous activation post-operatively and the impressive tachycardias which followed any operative procedures on these cases. This in our early experience with hyperthyroidism in very young children, made us fear to undertake operative procedures on them. With this in mind, we tried first iodine and x-ray on a number of these cases without any satisfactory success and we now wish to make it clear from our experience that hyperthyroidism in children is just the same as hyperthyroidism in adults. We approach it surgically from just the same viewpoint as we do hyperthyroidism in adults. The end results are just as good, the dangers are, however, I think, a little bit greater, and I speak now particularly of the very severe cases.

There are two points which are of practical interest about which we have learned as the result of practical experience in dealing with the surgery of hyperthyroidism in children, and they are: one, that children have such a

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great capacity for intense toxic reaction post-operatively that we think in the very intensely toxic cases in children, it is always wiser to divide the operation into two stages, doing a right subtotal thyroidectomy first, sending the child home for six weeks, then having them back and doing a left subtotal thyroidectomy. This procedure, as in adults, may be one of hypercaution but certainly, when one deals with a condition such as hyperthyroidism in children in which the mortality rate is a little higher than with adults, it is, I believe, wise to be on the safe side.

The other feature concerning hyperthyroidism in children, particularly young children is the matter of the amount of thyroid tissue to be removed.

In adults, the penalty for removing too much thyroid tissue and producing myxedema is not very great since artificial thyroid feeding is almost a complete and satisfactory substitute for natural thyroid secretion. In children, however, thyroid secretion is not only necessary for the maintenance of metabolism but is also essential for developmental effects. For this reason, the penalty for the production of myxedema in a very young child may very definitely be of more serious consequence than that in adults. With this in mind, we have taken the position that when one does subtotal thyroidectomy in particularly young children, a larger remnant of thyroid than in adults should be left behind to guard against the possibility of the production of myxedema.

I wish now to speak of a typical type of hyperthyroidism which we have for practical purposes, termed "apathetic hyperthyroidism."

There are two types of hyperthyroidism or exophthalmic goitre with one of which everyone is familiar, that is, the typical activated exophthalmic goitre which is so characteristic of the disease, typified by exophthalmos, goitre, tachycardia, tremor, flushed skin, activation, rapid pulse and so forth. No one can mistake the diagnosis in a frank case of activated hyperthyroidism of this type.

We have often said that activated hyperthyroidism of this type when fully developed, can be diagnosed by the merest tyro. Not alone is this true but the condition so flies its own danger signals that one is always impressed with the seriousness of this state.

We have from time to time written, however, of another condition of hyperthyroidism which we have termed "apathetic hyperthyroidism."

There has been some criticism concerning the employment of the term "apathetic hyperthyroidism" and such criticism, I believe, is logical. It has been stated that apathetic hyperthyroidism is no different in origin than activated hyperthyroidism and that it is one and the same disease except that it occurs in the aged and that it has existed usually in a chronic state over a considerable period of time.

The above is true but we have particularly coined the term "apathetic hyperthyroidism" not because we wish to establish any new entity, but because we believe that by marking this group with such a term that so aptly describes it, attention may readily be focused upon it, it may thus be diagnosed more often and earlier and this condition is very frequently overlooked, due to the fact that apathetic hyperthyroidism is so non-obvious in its symptoms. Furthermore, we have particularly desired to call attention to this group under a separate heading, such as apathetic hyperthyroidism, because we feel certain that the operative seriousness of this group is not fully appreciated and if we can call attention to it by describing it by its outstanding feature, apathy, then not only can we perhaps make it easier to diagnose but also be more certain that the seriousness of such states will be appreciated.

Apathetic hyperthyroidism differs from activated hyperthyroidism primarily in the fact that patients with typical hyperthyroidism are agitated and activated while patients with apathetic hyperthyroidism tend to be calm, slow and even, as the term suggests, apathetic. Patients with acti-

vated hyperthyroidism of the typical type tend to have striking eye signs such as stare, diminished frequency of winking and exophthalmos. Patients with apathetic hyperthyroidism tend to have calm eyes with none of these signs. Patients with activated hyperthyroidism tend to have a large, firm thyroid gland. Patients with apathetic hyperthyroidism tend to have firm but small and pebbly thyroid glands. Patients with activated, typical hyperthyroidism tend to have a pounding apex beat, as we have frequently said, diffused over the entire precordia, while patients with apathetic hyperthyroidism tend to have no striking apex beat. The pulse rate in patients with primary hyperthyroidism is high. The character of the pulse is toxic. The pulse rate in apathetic hyperthyroidism is persistently but moderately elevated and is not toxic in character. The skin in the patients with activated hyperthyroidism is hot, soft and flushed. One is particularly apt to be impressed that when an elderly patient has activated hyperthyroidism, she appears much more youthful due to the soft, hot, flushed skin which is associated with activated typical hyperthyroidism. The skin in patients with apathetic hyperthyroidism, however, is cool, pigmented and wrinkled. What the cause of the pigmentation is, we are unable to say but following the relief of hyperthyroidism, this pigmentation usually disappears. The basal metabolism in activated hyperthyroidism tends to be markedly elevated. The basal metabolism in apathetic hyperthyroidism is elevated but only moderately so. One of the outstanding features of apathetic hyperthyroidism is weight loss. Many of the patients with apathetic hyperthyroidism have lost fifty, sixty and even one hundred pounds in weight but over such a number of months or years that the patient is not impressed with the seriousness of it.

When fatalities occur in apathetic hyperthyroidism and activated hyperthyroidism, they are of a distinctly different type. Should a patient with activated hyperthyroidism of the typical exophthalmic goitre type die, he will die in delirium, thrashing about in bed, sweating and with uncountable pulse rates.

Should a patient with apathetic hyperthyroidism die, however, for example, following too much surgery as complete subtotal thyroidectomy, he will frequently go back to bed with a very reasonable pulse rate, one hundred and twenty, of good quality, and not toxic in character, he will become drowsy, apathetic and finally comatose and die peacefully with no evidence of activation whatever.

Patients with activated hyperthyroidism, as has already been stated, impress one as being very serious risks while patients with apathetic hyperthyroidism run frequently excellent pulse rates on the table, only to go back to bed following operation and die very unexpectedly.

So impressed are we with the seriousness of the apathetic hyperthyroidism which so frequently occurs in people of advanced years, that when we are certain that hyperthyroidism is of this type, we unhesitatingly divide the operation of subtotal thyroidectomy into two stages.

One should, I think, be suspicious of apathetic hyperthyroidism in all patients who have a persistent, long standing, unexplained myasthenia. One should be suspicious of apathetic hyperthyroidism in all patients who run moderately but persistently elevated pulse rates which cannot be explained otherwise and one should be suspicious always of apathetic hyperthyroidism in patients who have had marked weight loss over a long period of time which cannot be explained.

What are the end results in subtotal thyroidectomy for patients with apathetic hyperthyroidism as compared with those with activated hyperthyroidism? They are equally as good. The lost weight is regained, myasthenia disappears, the pigmentation disappears from the skin, these patients who appear so elderly due to weight loss and wrinkling of the skin, following their recovery from this type of hyperthyroidism drop a number of years from their facial appearances and appear much younger. The end results in subtotal thyroidectomy in the patients with apathetic hyperthyroidism are just as excellent as in those

with subtotal thyroidectomy for activated hyperthyroidism. The two features with which I wish particularly to impress you are that due to the lack of obvious symptoms they are often not diagnosed and due to their moderate course while on the operating table, their seriousness is often overlooked.

I wish now to say a few words concerning the dangers of exophthalmos in patients with so-called exophthalmic goitre or primary hyperthyroidism and I am prompted to make these remarks because we have seen six eyes lost from a severe degree of exophthalmos in patients of this type.

One should realize that any patient with marked exophthalmos needs only to have an ulcer of the cornea to produce œdema, increased lid pressure and finally slough in the eye which will result in the need for enucleation of the entire eye.

One should realize that the cornea of the eye has no real blood supply and that its nourishment is received largely by osmosis. If one now has extreme exophthalmos resulting in severe pressure from the lid edges, due to the protrusion of the eye, the nourishment of the conjunctiva is interfered with and in addition to that the drying which results from diminished frequency of winking, also predisposes to injury of the cornea in these cases with marked degrees of exophthalmos.

One should realize also in preparing patients with exophthalmic goitre for operation that when preliminary narcosis is given, these patients are half asleep, often not fully conscious of what is going on and that it is easily possible for them to rub the sleeve of their nightgown across their prominent exophthalmic eyes, produce an abrasion of the conjunctiva, ulceration, infection and in this way bring about so much œdema that increased lid pressure produces slough and the final loss of the eyes.

One should realize also that following subtotal thyroidectomy occasionally, exophthalmos which was only mod-

erate previous to operation becomes more and more prominent until it is of the serious type. This type of postoperative exophthalmos is most frequently associated with a minus degree of metabolism and associated postoperative myxedema. Fortunately, it is extremely rare but when it occurs it is a most distressing situation requiring very radical measures to remedy it.

One should, I think, bear in mind that any patient with extreme exophthalmos is a candidate for blindness, that they should be cautioned when out on the street to wear goggles and not to get foreign bodies in their eyes. They should be cautioned, when it is due to exophthalmic goitre, that they should submit to surgery as early as possible in order that regression of the exophthalmos may be brought about as early as possible.

When exophthalmos reaches such a degree of prominence that it endangers the eye itself from lid pressure, one may do two or three things. The lid edges may be sutured together and if they are sutured together, they should be denuded of their epithelium so that they will grow together; otherwise, the stitches employed in suturing them together will very soon cut out.

Doctor Howard Naffziger of the University of California in San Francisco has devised an operation which offers these cases of intractable exophthalmos the only real hope when they have reached extreme degrees. It consists in turning down a frontal flap of bone on either side of the skull, elevating the temporal lobe and unroofing the bony orbital canal. This results in decompression of the orbit, permits the eyes to sink back, relieves lid pressure and saves many of these cases. Dr. Gilbert Horrax in charge of the Neurosurgical Department in the Clinic, has operated on two such cases and has saved the eyes in both cases.

It is very important, I think, for me to call your attention particularly to the dangers of extreme exophthalmos and to the measures which can be utilized in saving the eyes when this intractable exophthalmos occurs.

Another type of hyperthyroidism of which I have frequently spoken and which I wish to discuss with you is the question of acute hyperthyroidism, or what we have termed, thyroid crisis. Everyone dealing with hyperthyroidism should remember that even patients with moderate degrees of thyroid intoxication can very quickly progress into such acute stages of hyperthyroidism that delirium, vomiting and extremely severe intoxication occur with the serious possibility of the development of a fatality.

If one appreciates the symptoms which indicate the onset of a rapidly intensifying degree of hyperthyroidism, measures can be taken to offset the effects of this state and thereby not infrequently patients' lives be saved.

If patients are permitted to progress into the acute stages of severe hyperthyroidism amounting to what we have termed thyroid crisis, then fatalities will occur in a considerable percentage of these cases regardless of what measures are employed to combat these states. We have often stated that the acute crises of hyperthyroidism are much like the critical situations in diabetes. If one appreciates the onset, for instance, of diabetic coma or even hyperinsulinism, measures can promptly be instituted which will prevent patients from progressing into serious states in these conditions. Likewise, if one appreciates, as we have already stated, the indications of intensifying hyperthyroidism which may amount to thyroid crisis, measures likewise can be undertaken which will prevent these patients from progressing into these states from which they cannot be extricated.

One should be suspicious of a possible impending thyroid crisis when there is an unexplained, persistent increase in the pulse rate. When patients with hyperthyroidism have been running pulses of one hundred and twenty and show progressive and persistently elevated rates, one should be suspicious of the approach of a thyroid crisis. When patients whose mental states are perfectly clear, show any mental changes, one should be suspicious that this is an early indication of the delirium associated

with an intensifying hyperthyroidism. One should realize that hyperthyroidism, just as is diabetes, is markedly intensified by a superimposed infection. Given a patient with a moderate degree of hyperthyroidism, any severe infection can so intensify this that the patient may be very rapidly converted from a patient with a moderate degree of thyroid intoxication into one with intense intoxication amounting to a thyroid crisis with delirium, diarrhœa, vomiting and uncountable pulse rate. Likewise, one should remember that hyperthyroidism is a disease of hypercombustion and when patients for instance, are vomiting they are distinctly upon a verge of a thyroid crisis. When they vomit, they are unable to take in fluids, they are unable to take in fuel—two very essential elements in combatting hypercombustion. If they do not have fluid and fuel but hypercombustion continues to go on, a vicious circle is established whereby the hyperthyroidism or intoxication is intensified and the factors, such as loss of fluid and fuel, are exaggerated thus again further intensifying the effects of the hyperthyroidism. One should remember also that diarrhœa accomplishes the same result; with ten to fourteen loose movements a day, the fluid and fuel loss is great, the hyperthyroidism is intensified and the two desirable elements which have to do with combatting hypercombustion, fluids and something to burn, are lost. We feel very strongly, therefore, that when one has a patient with hyperthyroidism and any of these indications of intensifying hyperthyroidism are present, urgent measures should immediately be undertaken to offset them and these measures consist of the introduction of fluids, fuel and iodine.

We have always appreciated that one of the best ways to offset the effects of the excessive hypercombustion associated with thyroid crisis is the introduction of salt solution and glucose intravenously. We used to employ, however, the ordinary method of introducing one thousand cubic centimeters at one sitting, and seventy-five to one hundred and twenty-five grams of glucose in the thousand

cubic centimeters of salt solution. This fluid is undoubtedly utilized very quickly in severe and intense hyperthyroidism and likewise, if it is introduced rapidly, some of the glucose is spilled over in the kidney and lost and the remainder rapidly burned so that there are periods perhaps during the twenty-four hours during which particularly fluid is not available for the patient in excessive stages of hypercombustion. This we have overcome by the employment of an intravenous drip method, utilizing the intravenous needle of Doctor G. A. Hendon of Louisville and setting the drip apparatus so that forty to sixty drops of salt solution containing five per cent glucose solution are delivered into the vein constantly.

We no longer introduce this intravenous needle into the median basilic vein because the arms are moved around so violently by delirious patients, the needle is disturbed, displaced and the introduction of the fluid is interrupted. We introduce the needle now into the long saphenous vein above the ankle, strap the rubber tubing down under the sole of the foot and along out by the great toe, then employ a large amount of slack tubing so that the patient can move his foot around even if delirious and not kink it. We used to employ a thermos bottle to keep the solution warm but patients with hyperthyroidism will heat their solutions sufficiently after they get into the vein and most of them have such degrees of excessive heat production that it is good for them to have moderately cool solutions introduced into their circulation. We have likewise learned that one should not employ ten per cent glucose solution since it tends to thrombose the vein. We have frequently used five hundred and more grams of glucose solution in these cases. These needles run day and night in the same vein for four days on an average without requiring changing. We have had one needle run eleven days the twenty-four hours around delivering forty to sixty drops per minute without requiring change. This, however, is exceptional.

While fluids and fuel in the form of glucose, are extremely essential in the treatment of acute hyperthy-

roidism, so also is iodine. When we first began to treat these patients in thyroid crisis, we were at a loss how to satisfactorily introduce iodine into the circulation. If they were vomiting or had diarrhœa, it could not be satisfactorily given by mouth and for a while sodium iodide intravenously was suggested as a method of supplying iodine in these cases. We have now learned that one can introduce directly into the salt solution which is given intravenously, fifty minims of Lugol's solution daily with no bad effect. It is thus delivered effectually into the circulation where it is needed and if there be a cardiac complication, digitalis likewise can be added to the salt solution.

I would again like to stress the need of appreciating the onset of increasing thyroid intoxication and the presence of an impending thyroid crisis and also impress upon you the fact that if urgent methods of treatment be undertaken, the majority of these patients cannot only be gotten out of crisis, but can be kept out of crisis, can then be put upon a high carbohydrate diet for two or three weeks and gotten in such good condition that a right subtotal thyroidectomy can be done upon them.

It used to be stated that one should not operate upon patients close to a crisis. It is true that one should not operate upon patients before they are out of a crisis but one should not fail to operate upon patients after they are out of a crisis. If these patients are sent home because one fears to operate upon them close to a crisis, some of them will definitely go back into a crisis again and it will not be possible to extricate them a second time. On the other hand, they are usually such serious risks that it is unwise to undertake subtotal thyroidectomy as close as three weeks to a thyroid crisis. In such cases, we do, as already stated, a right subtotal hemithyroidectomy, send the patient home for six weeks then have them back and do a left subtotal hemithyroidectomy. By this measure the course of the disease is interrupted and we are certain that they will not return again in a crisis.

We have repeatedly written on the subject of the association of hyperthyroidism and heart disease and I think it will be of interest to you in this connection for me to review some of our views with you on this subject. First of all, we have always been interested as to whether or not there was an actual thyroid heart. Doctor L. M. Hurxthal in the Medical Department of the Clinic has repeatedly stated that, based upon our observation of a number of thyroid fatalities post-operative and unoperated, we have never been able to determine that there actually was pathological evidence of a destructive action on the part of thyroid secretion on the heart muscle.

If one assumes that the enlargement of the heart, associated with tachycardia is due to the hyperthyroidism and not to work hypertrophy, then this may be a thyroid heart. If one assumes that auricular fibrillation which is so often associated with hyperthyroidism, is evidence of heart damage, then this likewise, as Dr. Hurxthal has stated, may be evidence of a thyroid heart but as far as actual microscopic evidence of heart damage as the result of prolonged hyperthyroidism goes, we have never been able to determine that such a condition exists; so we have felt that there is no true thyroid heart.

Auricular fibrillation is one of the most constant cardiac abnormalities associated with hyperthyroidism. Over eighty-five per cent of all the patients whom we have seen with hyperthyroidism and cardiac decompensation, have had auricular fibrillation. Auricular fibrillation is a most inefficient cardiac rhythm and when it persists in a heart which is already damaged and which is being overdriven by hyperthyroidism, there must constantly be the danger of cardiac failure.

As regards auricular fibrillation and hyperthyroidism, we know from our experience that after the removal of the hyperthyroidism and the employment of quinidin, eighty-five per cent of these patients can be restored to normal rhythm and will remain in normal rhythm.

Regarding the use of quinidin in auricular fibrillation in patients with hyperthyroidism, we have learned some definite things: One is that one wastes the quinidin effect if it be given before subtotal thyroidectomy. One can, in patients with hyperthyroidism and auricular fibrillation, give quinidin and in some of the cases, restore the rhythm to a normal character but upon doing a subtotal thyroidectomy, there will be such a post-operative reaction that absolute irregularity will again occur and the quinidin effect will thus be lost. For this reason, we have established a rule that quinidin is not to be given until five days post-operatively by which time the patients have passed through any thyroid storm or reaction and then when their rhythm is restored to normal rhythm with quinidin, in eighty-five per cent of the cases it will remain normal.

The association of hyperthyroidism and heart disease and the ability of patients with hyperthyroidism and congestive heart failure to stand surgery is to my mind and always has been a most fascinating subject. We have written a great deal about it. We designated this group of cases as thyrocardiacs. We have operated upon a great many of them and have been deeply interested in this field.

I have thought a great deal about this field and often have wondered why patients with such serious cardiac decompensation could withstand surgery as well as they have with such a low mortality rate. We have now operated on three hundred and twelve of these thyrocardiacs with a mortality of only four and six-tenths per cent, not a serious death rate in view of the severity and seriousness of this condition.

The reason that these patients stand surgery as well as they do is not apparent on the surface. It is due to the fact that they are automatically segregated into those who will stand surgery and those who will not before they come to us for consideration. When a patient has very little cardiac reserve and hyperthyroidism is superimposed upon this excessive degree of cardiac damage, he dies and

does not get to us for consideration as to the question of thyroid surgery. When, on the other hand, he is able to get to us or even to live long enough so that his physician and he consider the question of thyroid surgery, he or she of necessity must have a considerable cardiac reserve; otherwise, the burden of the superimposed hyperthyroidism would bring about such cardiac disability that the question of operation could not even be considered. When patients have sufficient cardiac reserve so that the question of operation can be considered, then it is of such an amount that when the hyperthyroidism is removed, they have a surprising capacity for activity.

We have recently reported our end result studies in two hundred and fifty-six of these cases followed from one to ten years. Of that number with hyperthyroidism and cardiac decompensation, over ninety per cent have regained their compensation and retained their compensation so that they are able to be up and about and active. Of all the two hundred and fifty-six cases whom we have been able to find and follow over this period of one to ten years, complete disability now exists only in three cases.

This too is explained by the fact that when patients do not have considerable cardiac reserve, there is not the question of disability but a fatality results.

One can, therefore, say regarding the cases of hyperthyroidism and cardiac complications that the most common cardiac complication is auricular fibrillation, that over eighty-five per cent of these cases following surgical removal of their hyperthyroidism and the employment of quinidin can be restored to normal rhythm, that in a follow-up study of two hundred and fifty-six cases of cardiac decompensation and hyperthyroidism, over ninety per cent have had their compensation restored and their hearts have remained competent over a period of from one to ten years following subtotal thyroidectomy and this with a respectable mortality rate of four and six-tenths per cent.

I wish now to speak of another common complication with which, due to our association with Dr. Joslin in the New England Deaconess Hospital, we have had experience in a number of such cases and that is the association of hyperthyroidism with diabetes. Hyperthyroidism superimposed upon a patient with diabetes is a very undesirable complication since it interferes definitely with the management of his case, it diminishes his tolerance for carbohydrates, increases his demand for insulin and makes the dietary management of his case, due to hypercombustion, difficult.

We have learned that the mortality of the surgery of hyperthyroidism when associated with diabetes is a little bit higher than in a patient who does not have diabetes but being between three and four per cent is within reasonable limits.

We have learned in connection with these cases that there is an increased incidence of glycosuria in patients with hyperthyroidism and that following the relief of hyperthyroidism, this glycosuria disappears. We have likewise learned that the removal of hyperthyroidism in no case has resulted in a cure of the diabetes. One can say as the result of an experience now amounting to well over a hundred and seventy-five cases of hyperthyroidism associated with diabetes that there will be a definite increase in carbohydrate tolerance, that there will be a definite diminution in the need for insulin and that the management of the diabetes will be very much less difficult.

Patients with diabetes and hyperthyroidism should be submitted to surgery not only because of the dangers of the hyperthyroidism but because of the added difficulty in managing the diabetes.

One should have in mind that with the added mortality in this complication, more two stage operations should be done in patients with hyperthyroidism and diabetes than in those with hyperthyroidism alone.

Finally, the last subject of which I wish to speak in connection with hyperthyroidism is that of the association of hyperthyroidism and pregnancy.

It used to be said by the obstetricians that when a patient had hyperthyroidism and pregnancy, the uterus should be emptied. That is not our present feeling. We know that if patients who are pregnant and have hyperthyroidism are permitted to go into the last stages of pregnancy, very serious complications may arise.

We know that if patients with hyperthyroidism have to be given general anesthetics and have major surgical operations performed, in many of the cases as the result of operative trauma and post-operative reaction the hyperthyroidism may be so intensified that a fatality from the hyperthyroidism results. If, then for example, a patient be permitted to go into the late stages of pregnancy and Cesarean section or prolonged labor, requiring instrumental delivery becomes necessary, a fatality as the result of the intensified hyperthyroidism may eventuate.

Our attitude today in the treatment of patients with hyperthyroidism and pregnancy is that they should be submitted to subtotal thyroidectomy at the earliest possible date in their pregnancy. This then relieves them of the hyperthyroidism and if difficulties arise at the time of their labor, there is not the danger then of the establishment of acute thyroid intoxication and a fatality.

We have operated upon nineteen patients in pregnancy with hyperthyroidism. There have been no fatalities in the nineteen cases. One miscarried ten days after operation after driving two hundred miles home from the hospital. This hardly can be attributed to the operation and I do not believe that there is any particular danger of difficulty with the baby in relation to the operation of subtotal thyroidectomy for hyperthyroidism in pregnancy. We, therefore, strongly urge that when patients who are pregnant have hyperthyroidism, the diagnosis be made and the operation be performed at the earliest possible date in their pregnancy.

I have tried to present to you the various aspects of hyperthyroidism from the practical point of view from our own experience with the condition and I think perhaps you would be interested in what the mortality rate has been in the Clinic dealing with these cases.

We have now done something over twelve thousand thyroid operations. The mortality rate in exophthalmic goitre has ranged from eight-tenths of one per cent down to one-tenth of one per cent last year. Last year was our most successful year because we operated upon one thousand and twenty-one goitres with but one death. One should recall, however, that the mortality of toxic adenoma will always be higher than the mortality of primary hyperthyroidism, one and eight-tenths per cent in our experience, due to the greater age of these patients. The mortality in adenoma and the various other thyroid states is almost of trivial amount.

One should also remember that the mortality rate in thyroid surgery will never be the same as the mortality rate in hernia, fibroid operations, appendicitis and various other general surgical conditions. Thyroid surgery is not a type of surgery which can be done casually. When it is done casually the mortality will be prohibitively high. When, on the other hand, it is done by organized groups with good medical preparation, with good technical operative assistants, with good anesthesia and with good post-operative care, the mortality will be low and the eventual results as satisfactory as following any operation in surgery.

MINERAL METABOLISM*

JOSEPH C. AUB
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In no constituents of the body is the so-called "homeostasis" of Cannon more strikingly maintained than in the inorganic salts. These salts are composed of a number of bases and a number of acid radicles, which respond in an accurate, coordinated way so that they balance each other, not only to maintain the pH of the body but also to help maintain the constant osmotic pressure of tissue fluids. In the body, because of the great efficiency of the normal kidney, an excessive intake of either acid or base can be readily eliminated. By such means as this the body cells are bathed by a solution which remains extraordinarily constant in salt content. Probably the content of no substance remains so constant in the body tissues as do the inorganic bases. Normally at the level of 150-160 milliequivalents it varies only very rarely as much as 10 milliequivalents from the normal. It is obviously of enormous importance to keep the bases in the blood at a constant level, a level which is not far removed from the concentration of base in sea water at the time when we are supposed to have emerged from it. In order to maintain this constant level it is essential that water and salts should fluctuate together, so the generalization can be made that in disease, when excess base is lost by excretion, water is also lost and dehydration follows; when base is retained, so also is water, and edema results.

One of the striking and unexplained phenomena of the salts in the body is the distribution of base. Sodium is the predominating base of all the fluids outside of the cells, while potassium predominates inside all of the cells. As a result, when fluids are lost from the body it is largely

* Delivered October 25, 1933.

sodium salts which are excreted. This is well illustrated by the fluid losses in burns, diarrhoea, or excessive vomiting. Here the body becomes depleted of its sodium salts so that they must be replenished.

On the contrary, when body cells are broken down there is a depletion of potassium salts. This may be seen in starvation, where breakdown of tissue is associated with a mounting elimination of potassium through the kidney. At the same time, the excretion of sodium from extra-

TABLE I.

URINARY EXCRETION DURING FASTING*

Days of Fast	Calcium gms.	Potassium gms.	Sodium gms.
2-4	.24	1.37	.93
5-6	.27	1.45	.28
10-11	.22	1.01	.10
18-19	.25	.68	.05
24-25	.17	.79	.06
30-31	.14	.61	.05

cellular fluids falls to a very low level so that the total base content of the blood plasma remains constant (Gamble, Ross, and Tisdall[1]) even after a prolonged fast. Remembering that it is essential to health to maintain the normal salt concentration in the body, as well as to maintain a normal volume of blood, let us see what happens superficially in two diseases in which these levels are sorely strained, namely, intestinal obstruction and nephritis.

The work of Gamble and McIver[2] has taught us much in regard to the effects of intestinal obstruction. The gastric juice contains not only a large amount of hydrochloric acid but also a considerable amount of sodium. Bile and pancreatic juice also have as much sodium in them as has the blood serum and they are alkaline in reaction. This large amount of base and of chlorine ions, which is poured into the intestinal tract, is reabsorbed in health, but in certain clinical conditions they may be lost. Thus, ex-

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*Taken from Benedict, F. G., A Study of Prolonged Fasting, Carnegie Institution of Washington, 1915.

cessive vomiting with or without intestinal obstruction, or bile fistulae, or even severe diarrhoeas are all associated with a loss of base and of chlorine. The importance of these secretions in regard to fluid as well as salts is well illustrated in the work of Rowntree.

TABLE II.

AN ESTIMATE OF THE RELATIVE DAILY VALUES OF SECRETIONS POURED INTO THE INTESTINAL TRACT OF MAN*

	cc.
Saliva	1500
Gastric juice	2500
Bile	400
Pancreatic juice	600
Succus entericus	3000
	8000
Total blood plasma	3500

* Taken from Rowntree, L. G., *Physiol. Reviews,* 1922, II, 116.

It is dramatically evident, when one compares the total volume of blood plasma to the daily volume of intestinal secretions that a precarious situation may result from the loss to the body of these secretions. If the vomiting is gastric, there is more chlorine lost than base, if it involves the bile and pancreatic secretion there is apt to be an excess of base lost in the fluid.

So as not to complicate the problem too much, let us consider pyloric obstruction alone, which has been well studied by Gamble[2]. The loss in this condition is largely hydrochloric acid and sodium. This loss may be great and is complicated by the obvious inability of the body to replace this loss by eating. There follows a greater loss of chlorine than of sodium. As a result, there is a tendency to an alkalosis with the resulting picture of "gastric tetany." Chlorides in the blood may fall to less than half the normal concentration (McVicar, C. S.[3]), a loss which is far greater than that of base. The body can stand this disproportionate loss very poorly and, therefore, gets back to a relative balance by excreting more base by urine. The result is a very marked fall in base as well as chlorides

in the plasma. This condition demonstrates dramatically how essential are inorganic salts to health, for there is a rapid appearance of the picture of intense dehydration, diminished urinary output, nitrogen retention, with an eventual collapse and death. The treatment for it is simple and is the same for all of the diseases in which excessive intestinal contents are lost: sodium chloride and water in adequate amounts. By adequate amounts is meant enough to cause a good flow of urine so that any excess of chlorides or of base are separately dealt with by the kidneys. No other treatment seems an adequate substitute. Water alone, or soda bicarbonate alone, or glucose (Walters, W. and Bollman, J. L.[4]) or ammonium chloride are not satisfactory (Gamble, J. L. and Ross, L. G.[5]), for all three of the essential substances which have been lost must be replaced, and water, sodium, and chloride must be given. With adequate kidneys, a fairly rapid adjustment is made and the components which are given in excess are excreted while those sorely needed by the body are retained. A similar situation has recently been demonstrated in Addison's disease (Harrop[6]).

The lavish loss of water and sodium and chloride, which may result from intestinal abnormalities, is in great contrast to the work of the kidneys. In the secretion of urine by normal kidneys, each inorganic component of the plasma is excreted only when present in excess. As a result, the normal kidney maintains a quite constant environment for the body cells, as long as the various constituents are adequately supplied. With kidney damage, however, the accuracy of the mechanism may be lost and salts and water may be retained or excreted in excess. This is soon followed by symptoms.

In the edema of nephrosis, the reduction of the plasma proteins plays a most important part which cannot be discussed this evening. However, the inorganic salts are also seriously involved for where there is edema there is retention not only of water but also of sodium and chloride. We

speak clinically of chloride retention, meaning retention of inorganic salts. This term is used because of the fact that the chemical analysis for chlorides is simpler than that for base. It is probable that sodium has far more to do with edema than has chloride retention. Good evidence for this lies in the tendency to retain water when sodium bicarbonate is given and to produce diuresis when ammonium chloride is administered. All of the retained salts and water stay in the tissues, for Van Slyke[7] has shown that the volume of blood plasma in edematous patients is quite normal, while Peters has shown that the total base in the blood plasma is usually lower than normal (Peters, J. P., Wakeman, A. M., Eisenman, A. J., and Lee, C.[8]).

The retention of sodium, chloride, and water is not the invariable result of kidney damage. In fact, in the advanced stages of nephritis, where large quantities of dilute urine are excreted, sodium and chloride may be washed from the body. Under such conditions, Peters[8] has found that the total content, as well as concentration, of sodium salts in the body may be definitely reduced and with this, of course, is associated dehydration.

From the point of view of these findings, it becomes obvious that the treatment of nephritis will vary according to the condition of the body fluids. In patients with edema and stored sodium chloride, salt intake should obviously be restricted, but in nephritics where dehydration from polyuria is marked the ingestion of adequate salt is indicated and needed.

What has been said, in both of the abnormalities discussed, suffices to bring out the fact that the primary inorganic salt involvement in volume changes of extracellular fluid has to do with abnormalities of sodium and of chloride. In changes which involve body cells, however, as in starvation, the important loss from the body is the predominating base of tissue cells, potassium.

So far, this discussion has referred to the salts of the soft body tissues. These salts exist only in the necessary concentration in the active protoplasm of cells and the fluid which bathes them. There is no large storehouse of these salts. If they are lost from the body the sole source of replenishment is from food or medication. However, there is one large storehouse for inorganic salts from which, in time of need, large quantities of base and acid can be drawn. The bones, in this regard, resemble the fat storehouses in the caloric requirements of the organism. The role of calcium and of phosphorus is, therefore, of interest in two ways: first, in their deposit in the bones and, secondly, in the liberation from the bones to satisfy the needs of the organism as a whole.

In the metabolism of bone we clinicians are apt to speak too simply of calcium metabolism. It must be remembered that phosphates are fully as important as is calcium. This is quite well recognized now in rickets where an inadequate phosphate intake may be of prime importance. An excellent example of this is found in the work of Theiler[9]. He studied the disease of Lambsiekte in cattle on the South African veldt. These herbivorous animals had the extraordinary habit of eating the bones of dead animals of their own kind. Theiler found that this proved lethal because of a botulinus infection which was spread by this osteophagia. Why should herbivorous animals eat bones? This he found was due to a deficiency of phosphorus in the grasses used for grazing, and, by making adequate amounts of inorganic phosphates available to the cattle, he promptly caused osteophagia to cease. This discovery was of great economic, as well as scientific value. It serves as an excellent example of the need of the body for phosphates, a radicle equally as important as calcium, to which it is so closely related.

Calcium and phosphorus metabolism differ from the other inorganic salts because they are continuously going in and out of the bones, and are continuously being excreted, even in starvation. If the normal level of calcium

in the blood is changed, effects are seen in muscle tone. A low blood calcium, below 7 mg. per cent, is associated with an increased neuromuscular irritability, or tetany. A high blood calcium leads to low muscle tone, an increased calcium excretion, and abnormal changes in the bones and kidneys.

The maintenance of this normal calcium level is more complicated than that for sodium, for several factors other than the kidney affect it. First, there must be adequate absorption of calcium. This is obviously difficult and in certain diseases like steatorrhoea or Gee's disease it cannot be adequately accomplished. In this digestive disease there is difficulty in absorbing fats and soaps, resulting in the excretion of insoluble calcium soaps in the bulky diarrhoea, thus preventing the absorption of calcium into the body. The result is a gradual thinning of the bones with the development of osteomalacia, and an eventual fall of the blood calcium and tetany. Vitamin D improves the absorption of calcium from the intestine and in very large quantities will relieve this condition.

Except for this effect of Vitamin D, little is known of the factors which influence the absorption of calcium. Once absorbed, calcium may either be deposited in the bones or excreted. The retention in the bones may be large, certainly as much as a gram a day for short periods. This storehouse, however, is not an inert deposit, for the bones are continuously giving up and replacing their salts, and there is good evidence that calcium probably leaves one part of the bones to be redeposited in other parts. How this calcium is deposited and liberated is not always clear. Certainly, there are cells—the osteoblasts, associated with new bone formation; and the osteoclasts, associated with the absorption of bone tissue. Osteoclasts are described in bone which is being depleted by parathyroid hormone[10], and in hyperthyroidism[11]. It is not known whether bone salts can be absorbed or deposited without the presence of these cells. It is hard to believe that the ingestion of acid salts, which increase calcium excretion, causes this

liberation from bones by the activity of osteoclasts, but this problem is not yet settled. At any rate, bone salts are easily pulled from or deposited in the bones. The chief seat of this calcium storehouse is in the bone trabeculae near the epiphyses. These trabeculae can easily be depleted by a low calcium diet and can be replaced by increasing the calcium intake. The bone shafts are less seriously involved, though recent work has indicated that they may also show microscopic evidence of absorption in hyperparathyroidism and hyperthyroidism[10, 11].

What are the known factors which influence this store and influence the level of calcium in the blood? They include internal secretions, vitamins, and foods.

The parathyroid glands are probably the most important of these factors in the normal regulation of the body calcium. Their primary influence seems to be upon the level of blood calcium and phosphorus. From a normal level of 10 mg. per cent, the calcium falls after parathyroid extirpation to 4 or 5 mg. per cent. Signs of intense tetany develop in about twenty hours, when the blood calcium has fallen below 7 mg. per cent.

The lowered serum calcium causes intense irritability of the neuromuscular mechanism and the laryngeal and muscular spasms and generalized convulsions are evidence of this. Calcium excretion on a low calcium intake falls to a minimum. When parathormone, the active principle of the parathyroid gland, is injected intramuscularly there is a latent period of four hours, after which the blood calcium rises and tetany disappears for approximately twenty hours.

If an overdose of parathormone is given, or with an overacting parathyroid adenoma, the blood calcium rises above normal and may even reach 20 mg. per cent. This condition of hyperparathyroidism is being described to you later by Dr. Jaffe. Here, therefore, it need only be said that the amount of calcium absorbed from the intestines is not influenced by parathormone and that the increased

calcium in the blood and urine, resulting from overdoses of the hormone, comes from the bones. This is evident from the experimental work of Jaffe and Bodansky[10], which showed bone changes even with probably adequate calcium in the food. With very high calcium diets, however, these cases can be maintained in calcium equilibrium[12] or even a positive balance. What the bones would then show I do not know. It is interesting that an immunity develops towards commercial parathormone, prepared from cattle, so that after several weeks or months of use the blood calcium sinks back to its original level. This must be an immunity to a foreign protein, for no such immunity follows the oversecretion of a parathyroid tumor. One such case, of twelve years' duration, is known to have maintained a high blood calcium for the last seven years of the disease.

The action of parathormone is mimicked in every way by large doses of Vitamin D. This was first pointed out, I think, by Porges[13], who cured a chronic case of tetany by means of viosterol. Taylor, Weld, Branion, and Kay[14] also showed this close relationship and recently Kozelka, Hart and Bohstedt[15] have shown that parathyroidectomized puppies can reach maturity and can raise normal offspring by the use of large doses of viosterol. The differences seem to be that viosterol aids in the absorption of calcium from the intestine, and its effect lasts for days, while parathormone lasts for only a matter of hours. It is important to remember that a high blood calcium level is nearly always due to overactivity of the parathyroid glands or to overdosage with vitamin D. I think there is also a very rare case associated with an excess of protein in the blood. A low blood calcium level means parathyroid or vitamin D deficiency, or a deficient calcium absorption. Calcium is also somewhat reduced when plasma proteins are low (Peters). Although the parathyroids and vitamin D are the factors which affect *blood* levels of calcium, they are not the only influences which affect calcium metabolism. Abnormal calcium *excretion* can be stimulated by other

means. The thyroid hormone is an important influence, since oversecretion of the thyroid gland increases the excretion of calcium enormously, while in myxedema the demands upon calcium stores are markedly reduced[16]. The thyroid secretion exerts no effect upon the normal level of blood calcium. Its action rather seems to stimulate the catabolism of bone, which results in excessive excretion.

An acid diet is the last factor I want to speak of, for a large excess of acid can increase the excretion of calcium approximately as does parathormone, but this factor again does not appreciably affect levels in the blood[17].

Table III shows the various laboratory combinations which are important in diagnosis.

TABLE III.

ANALYTICAL FINDINGS IN VARIOUS TETANIES AND RELATED DISORDERS

DISEASES	BLOOD PLASMA VALUES: Calcium	Phosphorus	pH	Phosphatase*	EXCRETION DURING LOW CALCIUM DIET: Urine Ca	Urine P	Feces Ca	Feces P
Tetany due to Parathyroid deficiency	low	high	normal		low	low	normal	normal
Hyperparathyroidism	high	low	normal	high	high	high	normal	normal
Steatorrhea—Difficulty in absorbing calcium from the intestines	normal or low	low	normal	normal or slightly high	low	high	high	normal
Osteomalacia from Deficiencies and Rachitis	normal or low	low	normal	high	low	low	low	low
Hyperthyroidism	normal	normal	normal	high	very high	very high	high	high
Paget's Disease (Osteitis Deformans)	normal	normal	normal	very high	No marked variation			
Gastric Tetany	normal	normal	increased					

* See Kay, Physiological Reviews.

From these factors the treatment of low calcium tetany is clear.

1. A high calcium diet, possibly with added acid salts like ammonium chloride.

2. Intravenous or intramuscular use of calcium gluconate for immediate effect. For more lasting effects which, however, are not obtained for some hours, one should employ No. 3.

3. Large doses of viosterol to raise the blood calcium level. Because no immunity develops to this, it is preferable to No. 4.

4. Parathormone.

5. Thyroid medication, which is well worth remembering.

To practitioners of medicine, I cannot abstain from mentioning the importance of calcium during pregnancy. It has been shown by Schmidt[18] and others that an enormous amount of calcium can be stored in the bones during pregnancy. That it is important to accomplish this by a high calcium diet throughout pregnancy is self evident, when one realizes that a negative calcium balance can probably not be avoided throughout the period of lactation. Further evidence of strain upon the calcium metabolism is indicated by the interesting work of Kozelka, Hart, and Bohstedt[15]. Their parathyroidectomized dogs could be maintained with a normal blood calcium by daily doses of 14 rat units of vitamin D. During pregnancy, however, 4,000 to 26,000 were required and during lactation as many as 66,000 rat units were necessary. This extraordinary demand implies some mechanism which we do not yet understand.

It is also important to realize that several heavy metals behave in the body approximately as does calcium. Lead[19], mercury[20], and radium[21] are influenced by the same procedures that influence calcium. They are stored in the bones and are liberated from this storehouse in increased amounts when calcium is liberated. This offers a method

of treatment which allows the most readily available of these metals to be pulled from the bones and excreted[10]. The remainder is excreted very slowly, just as is calcium.

What is the interrelationship in body fluids of these ions which are stored, such as calcium and phosphates, to those which have no storehouse, like sodium and chloride? In the first place, the concentration of the calcium and phosphorus is relatively very small. Variations which double their concentration would not affect the total level of acid or base in the plasma more than occurs physiologically, and there does not appear to be much readjustment in other ions to such a change. These ions with low concentration in body fluids, may therefore cause dramatic signs and symptoms quite independently of other ions. Total base or chloride excretion is not influenced by the giving of parathormone, which dramatically increases the calcium and phosphorus elimination[22]. Thus, there is a good deal of independence of excretion of each of these substances and yet they remain closely related as a whole, keeping an accurate balance between acids and bases to maintain the normal pH of the body, and keeping normal the osmotic pressure and the inorganic salt environment—a group of substances which maintain a remarkable equilibrium in spite of the possibility of individual divergence from the norm.

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PROCEEDINGS OF ACADEMY MEETINGS

JANUARY

ANNUAL MEETING—January 4

I. Executive Session—Reading of the Minutes; Election of Fellows and Members; Presentation of Diplomas; Announcement re: Amendments to By-Laws introduced at the Stated Meeting of December 7, 1933.

II. Presentation of Annual Reports—(Read by title) The Council, The Trustees, The Treasurer, Committees.

III. Addresses of the Evening—a. Activities of the past year, Bernard Sachs; b. Presentation of Thomas W. Salmon Memorial Committee Report and portrait of Dr. Salmon, C. C. Burlingame; c. *Symposium on Encephalitis* with especial reference to the St. Louis outbreak; 1. Clinical and research aspects of the St. Louis epidemic, Ralph S. Muckenfuss, St. Louis; 2. Epidemiology, James P. Leake, Washington; 3. Recent research in the disease, Leslie T. Webster; 4. Clinical observations, Josephine B. Neal; 5. The importance of differential diagnosis, Frederick Tilney; 6. Discussion and summary, Thomas M. Rivers.

THE HARVEY SOCIETY (IN AFFILIATION WITH THE ACADEMY)—January 18

THE FOURTH HARVEY LECTURE, 'The Estrogenic Substances, E A Doisy, Professor of Biological Chemistry, St Louis School of Medicine

SECTION MEETINGS

SECTION OF DERMATOLOGY AND SYPHILOLOGY—January 2

I PRESENTATION OF CASES FROM a The Polyclinic Hospital, b The Good Samaritan Dispensary

SECTION OF SURGERY—January 5

I PRESENTATION OF CASES—a A new instrument for intestinal anastomosis, Henry Dawson Furniss, b 1 Raynaud s Disease—brachial periarterial sympathectomy without relief, 2 Raynaud s Disease—inferior cervical and second dorsal sympathetic ganglionectomy, 3 Thrombo angiitis obliterans—peripheral nerve alcohol injection for relief of pain, Beverly Chew Smith, c Three cases illustrating paper of the evening, Norman F Laskey (by invitation)

II PAPERS OF THE EVENING—a The relief of pain in thrombo angiitis obliterans by peripheral nerve section, Norman F Laskey (by invitation), Samuel Silbert, b Delayed and non union of fractures in the light of aseptic bone necrosis, Eugene J Bozsan

III GENERAL DISCUSSION—Howard Lilienthal, Samuel Silbert Frederic W Bancroft, Edwin A Spies.

JOINT MEETING—SECTION OF NEUROLOGY AND PSYCHIATRY and the NEW YORK NEUROLOGICAL SOCIETY—January 9

I PAPERS OF THE EVENING—a Clinical manifestations of female sexual deviations, Adolph Stern, b The question of psychic suicide, A A Brill, c Concepts and misconcepts about the principles of the psychoanalytic method, Karen Horney, Chicago (by invitation).

II DISCUSSION—Louis Casamajor, Monroe A Meyer, Gerald R Jameison, Marion E Kenworthy, Sandor Rado (by invitation)

SECTION OF HISTORICAL AND CULTURAL MEDICINE—January 10

I PAPERS OF THE EVENING—a Humorous sidelights in early prints on arthritis and gout (with lantern slides), Reginald Burbank, b Charles Darwin (1758 1778), Withering and the introduction of digitalis, John F Fulton, Yale University School of Medicine (by invitation)

II GENERAL DISCUSSION

SECTION OF PEDIATRICS—January 11

Papers by members of the Department of Pediatrics, New York University, and from Children s Medical Service, Bellevue Hospital

I DEMONSTRATION—Exhibit of enlarged colored transparencies of lung sections showing various forms of pneumonia, Charles Hendee Smith, Irving Graef, Elizabeth T Andrews

II PAPERS OF THE EVENING—a Anaphylactogenic properties of raw, heated, acidified and dried milks, Bret Ratner, Miss Helen L Gruehl, b Hematogenous dissemination in tuberculosis of childhood, Edith M Lincoln, c Paracentesis of the pericardium as a therapeutic procedure, Lucy Porter Sutton, d Serum treatment of pneumonia in childhood, Rosa Lee Nemir

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DEATHS OF FELLOWS OF THE ACADEMY

HIGHMAN, WALTER JAMES, M.D., 853 Seventh Avenue, New York City; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1905; elected a Fellow of the Academy January 6, 1910; died, January 24, 1934. Dr. Highman was a Fellow of the American Medical Association, a member of the County and State Medical Societies, the American Dermatological Association, the New York Dermatological Society, the Pathological Society, the Society of Associated Alumni of Mount Sinai Hospital. He was Dermatologist to Mount Sinai Hospital and Associate Dermatologist to Lenox Hill Hospital.

McAlpin, David Hunter, B.A., M.A., M.D., Hotel McAlpin, Broadway and 34 Street, New York City; graduated in medicine from Bellevue Hospital Medical College, New York City, in 1888; elected a Fellow of the Academy April 4, 1895; died, January 20, 1934. Dr. McAlpin was a Fellow of the American Medical Association, a member of the County and State Medical Societies, the National Tuberculosis Association, the Pathological Society and the Society of Alumni of Bellevue Hospital.

BUREAU OF CLINICAL INFORMATION

The Committee on Medical Education maintains at the Academy a *Bureau of Clinical Information* where detailed information may be obtained regarding opportunities for postgraduate medical study in Greater New York and in other cities of the United States, Canada and Europe.

A survey of postgraduate medical education in New York City has constituted one of the important undertakings of the Committee since its organization in 1924. The survey has been carried on from year to year with a view to improving the value of existing opportunities and encouraging the development of additional ones. To attain this aim the Committee has given its approval to those courses which after investigation have been found to be well organized, with adequate equipment and clinical material, and given by physicians of character who are known to be qualified teachers in their special lines of work. The result of each year's survey has been the preparation and publication of a *Synopsis of Approved Postgraduate Medical Courses Offered in Greater New York.* Copies of the Synopsis may be obtained on application to the Bureau.

The meetings, lectures, conferences, hospital rounds, and other interesting medical activities of the day are announced in a *Daily Bulletin.* The Bulletin, which is issued the previous evening, also announces the major operative work to be performed in the clinics of most of the important hospitals of the city. A *Bulletin of Non-Operative Clinics* held in more than thirty hospitals also is published. Copies of these Bulletins may be obtained at the Bureau and will be mailed to visiting doctors on request.

The Bureau maintains an approved list of clinicians who practice in foreign countries, and is prepared to answer inquiries from physicians who desire information regarding foreign medical men engaged in general and special practice.

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ACIDOSIS AND ALKALOSIS*

DONALD D. VAN SLYKE

For maintenance of normal physiological function, and of life itself, it is necessary that certain physical and chemical conditions in the body be kept constant within certain limits. Perhaps the most familiar constant of this sort is the body temperature. Ordinarily it is kept within a narrow range. When it deviates from this range changes in physiological functions result, such as the increased metabolic rate, pulse, respiration, and water loss that accompany hyperthermia. When the deviation becomes sufficiently wide, the lethal point is reached, where irreversible changes set in and death follows.

Another such physiological constant is the reaction of the blood. It is normally in the resting man expressed by a pH of 7.4, slightly more alkaline than water. The pH

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* Delivered October 25, 1933.

may be raised 0.2 or 0.3 above this level by such a simple physiological means as blowing off carbonic acid in voluntary overbreathing. And it can be lowered as much by the lactic acid produced in the muscles in a short, hard sprint. But if the change goes much farther in the alkaline direction the tetany of alkalosis sets in, nor can much greater change in the acid direction be tolerated without the symptoms of acid poisoning. The range within which life is continuously possible seems to be the narrow zone between pH 7 and 7.8. When we consider that some moulds can grow in 5 per cent sulfuric acid solution, it appears that the efficiency of our complicated and delicate organism has been bought at a heavy cost in cellular hardiness and adaptability.

The acid-base changes in the body are of two types, that caused by excess or deficit of carbonic acid, and that caused by excess or deficit of the supply of buffer alkali available for neutralizing non-volatile acids such as lactic, hydroxybutyric, and hydrochloric. The first type of changes we shall call carbonic acid excess and deficit, the second type we term alkali excess and deficit, because in it the alkali reserve of the body is increased or diminished. Discovery of the occurrence and significance of both types of changes was first made in the physiological laboratory and then found to apply to common clinical conditions. The [illegible]dvance in this field exemplifies the dictum of the elder H[illegible]aldane: "The physiology of today is the medicine of tomorr[illegible]ow."

Walter [illegible] in 1877 (50) studied in Schmiedeberg's pharmacological [illegible] laboratory the effect of administering hydrochloric acid to rabbits. He noted that when 1 gram of [illegible] per kilo [illegible] had been administered to rabbits there was [illegible]ea, tachycardia, and collapse, with lowering [illegible] ate of the blood to nearly zero. Walter [illegible] mplete description of the condition which [illegible] icit. A few years later Stadelmann (44) [illegible] nptom complex of diabetic coma greatly [illegible] id intoxication as revealed by the work

of Walter," and Kussmaul (24) saw the same similarity in the coma of terminal nephritis. These clinical observations led students of disease again back to the laboratory, where Minkowski (32) and Magnus-Levy (29) identified the intoxicating acid of diabetes as beta-hydroxybutyric, and Marriott and Howland (30) and Loeb and Benedict (27) showed that phosphoric acid and sulfuric acids produced in ordinary metabolism are retained in severe nephritis.

The opposite condition, the state of *alkali excess*, was produced experimentally by MacCallum (28), who caused dogs to lose hydrochloric acid from their bodies by ligating the pylorus and washing out the gastric juice. He found a marked increase in the blood bicarbonate, and eventual development of tetany. Since then it has become a common clinical observation that continuous loss of gastric hydrochloric acid by vomiting, whether caused by pyloric obstruction or other factors, results in a state of alkali excess, with a great increase in the bicarbonate of the blood and a decrease in the chloride.

The acid-base changes due primarily to respiratory over- or underventilation were also first noted in physiological experiments, and quickly found to be not unusual clinical occurrences. Grant and Goldman in 1920 showed that by voluntary overventilation they could produce an alkalosis of *carbonic acid deficit,* with development of tetany quite like that produced by loss of HCl or overdosage with sodium bicarbonate. A similar overventilation was soon observed by Harrop and Loeb (16) in encephalitis, has been found to be not uncommon in hysteria, and to a milder degree has been noted by Koehler (22) to be frequent in febrile conditions generally.

The tetany which accompanies the alkalosis of either alkali excess or CO_2 deficit appears to be connected with the pH increase in the blood, which occurs in both conditions. The symptoms are the same as in the tetany produced by lack of blood calcium. They occur when the pH exceeds 7.6-7.7, even though the calcium content is normal.

The acidosis of *carbonic acid excess* was produced in 1914 by Hasselbalch and Lundsgaard (19a), who caused animals to breathe the air containing CO_2, so that the concentration of free carbonic acid in the blood was increased. There was a marked depression of the blood pH, and a great hyperpnea, similar to that observed in Walter's experiments, in which the retained acid was hydrochloric. Later Dautrebande (7) and Meakins (31) found that there is a similar retention of CO_2 in some cases of emphysema and bronchitis, in which gas exchange in the lungs is markedly hindered, and in such cases dyspnea is present or readily produced by slight exertion.

The Blood Bicarbonate and Its Relation to the Available Buffer Alkali of the Body

The physiologically available alkali reserve of the body is in the form of buffer salts. These have the power of forming solutions, which with relatively little pH change, are able to neutralize the greater part of the acidity or alkalinity of added strong acids or alkalies. The manner in which buffers act is illustrated by the behavior of bicarbonate to which HCl is added. The reaction occurs:

$$NaHCO_3+HCl=H_2CO_3+NaCl$$

The effect is to replace the strong acid, HCl, with an equivalent of a weak acid, H_2CO_3, so that the hydrion concentration in the mixture of $NaHCO_3$, H_2CO_3, and NaCl is only a minute part of that which would exist if the HCl had remained free.

If, on the other hand, alkali instead of acid is added to a solution containing $NaHCO_3$ and H_2CO_3, the alkali reacts with the H_2CO_3 component:

$$NaOH+H_2CO_3=NaHCO_3+H_2O$$

In consequence the strongly alkaline NaOH is replaced by the weakly alkaline $NaHCO_3$. Thus a solution containing the buffer mixture, $NaHCO_3$ and H_2CO_3, can receive either strong acid or strong alkali with relatively small change in pH.

The neutralization of an acid or alkali by a buffer is not complete in the sense that the pH of the buffer solution remains entirely unchanged. If HCl, for example, is added to a $NaHCO_3$-H_2CO_3 mixture, the H_2CO_3 is increased and the $NaHCO_3$ is diminished, so that the pH becomes somewhat more acid, but the change is only a small fraction of what it would be if the HCl were added to an unbuffered solution (For a more complete account of the action of buffers, see [45*a*]).

In the body it is true that $NaHCO_3$ can almost completely neutralize invading acids, for the reason that the lungs can blow off the H_2CO_3 formed by reaction of the invading acid with bicarbonate. For the reason that its acid component can thus be removed almost instantly from the body, bicarbonate as a buffer offers a unique advantage over other buffers in the blood and tissues.

In the blood the chief part of the buffers is in the form of bicarbonate, the concentration of which is about 0.02 molar. About 0.01 equivalent more of alkali is available in the form of alkali hemoglobinate, which may be most simply symbolized as BHb. With these two buffers the 5 liters of blood in the body contain buffer alkali enough to absorb nearly 0.15 mole, or 150 c.c. of normal HCl, before the reaction becomes fatally acid. But the chief alkali store in the body is in the buffers of the tissues, which can neutralize about 5 times as much acid as the buffers of the circulating blood (46).

Although the blood bicarbonate contains only about 0.1 of the total available buffer alkali of the body, nevertheless it indicates the condition of the entire supply. For when an invading acid exhausts part of the blood buffer alkali with a fall in blood pH, the effect is divided with the buffers of the tissues bathed by the blood, so that the alkali reserve of all goes up and down together. The blood bicarbonate accordingly serves to indicate the state of the total alkali reserve of the body.

It has become customary to speak of the blood bicarbonate itself as the "alkali reserve." It is, in fact, a measuring-stick for the total reserve of the body, and as such the term "alkali reserve" may be applied to it.

In two other respects the bicarbonate and free carbonic acid of the blood have an especial significance. They are directly related on the one hand to the activity of the pulmonary respiration, and on the other to the actual reaction, the hydrion concentration or pH, of the blood. A 0.01 M solution of H_2CO_3 has an acid reaction, approximately pH 4, while a 0.01 M solution of $NaHCO_3$ has a definitely alkaline reaction of pH about 8. A solution with equal concentrations of both H_2CO_3 and $BHCO_3$ will have the intermediate pH of 6.1. The pH of any given mixture of H_2CO_3 and $BHCO_3$, in the presence of a physiologically normal concentration of total salts, depends on the ratio of $BHCO_3$ to H_2CO_3, as indicated by the Henderson-Hasselbalch equation (20):

$$pH = 6.1 + \log \frac{BHCO_3}{H_2CO_3}$$

(B=any base, Na, K, etc.). In the normal blood plasma $\frac{BHCO_3}{H_2CO_3} = \frac{20}{1}$ and the pH is 7.4.

Because of the relationship of the blood bicarbonate to the available buffer alkali supply of the body, to the respiratory regulation of the H_2CO_3, and to the vitally important pH of the blood, study of the blood bicarbonate gives more information about the state of the body's acid-base economy than observation of any other one value which can be easily determined. If the bicarbonate determination is coupled with that of the plasma pH, information is afforded which enables one to state whether the acid-base balance of the organism is normal, and if it is not, to diagnose whether the deviation is due to excess or deficit of alkali, or to respiratory loss or retention of CO_2.

The CO_2 Absorption Curve and the Acid-Base Diagram

The buffer alkali of the blood is partly combined with carbonic acid, and partly with hemoglobin, which acts also as a weak acid. When H_2CO_3 is present in ordinary concentrations, about 2/3 of the buffer alkali takes the form of $BHCO_3$, and 1/3 that of BHb. But if CO_2 escapes from the blood, so that the H_2CO_3 content decreases, some of the base shifts from $BHCO_3$ to the form BHb, in accordance with an approximate mass law equation:

$$\frac{BHCO_3}{BHb} = \frac{H_2CO_3}{HHb}$$

If ordinary blood is aerated so completely that all the free carbonic acid is removed, the bicarbonate completely disappears, all the buffer alkali shifting to the form BHb. Consequently, when the bicarbonate is determined as an indicator of the state of the acid-base condition of the body, it is necessary that the H_2CO_3 content of the blood be at a normal, or at least a known, concentration.

The behavior of the total CO_2, the $BHCO_3$, and the H_2CO_3 of the blood when the pressure of CO_2 in the atmosphere saturating the blood is varied, is shown by the carbon dioxide absorption curve in Figure 1. This type of curve was introduced by the elder Haldane for such studies of the blood, and is almost indispensable for graphic explanation of the conditions. It is seen that when the CO_2 tension, and the proportional concentration of dissolved free carbonic acid, represented as H_2CO_3 in the lowest slanting line, fall to zero, the total CO_2, including the $BHCO_3$, also falls to zero. At this point all the buffer alkali in the blood is in the form of alkali hemoglobinate, and a CO_2 or bicarbonate determination would lead to an interpretation that the alkali reserve had disappeared. It is only when the blood $BHCO_3$ or CO_2 content is determined with the CO_2 tension at a normal level that the $BHCO_3$ or total CO_2 content has significance as an accurate indicator of the acid-base balance of the blood and the alkali reserve of the body.

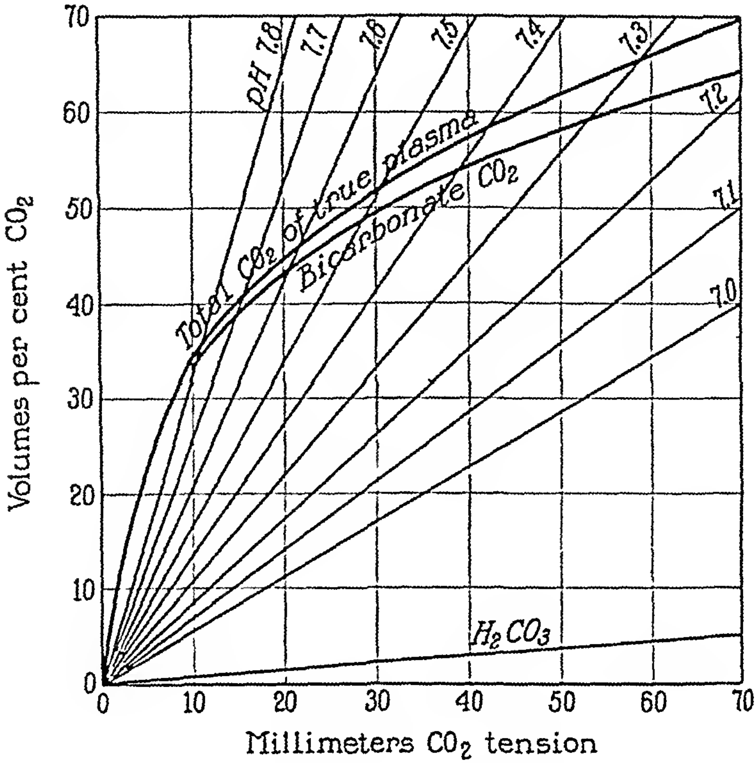

Fig. 1. Carbon dioxide absorption curve of true plasma of normal human blood. The ordinates represent the CO_2 content of plasma separated after the blood has been saturated with air containing CO_2 at the tensions indicated by the abscissae.

It may be desirable here to interject a word of explanation concerning the significance of the CO_2 tension and its relation to the H_2CO_3 content of the blood. The term "CO_2 tension" is used to express concentration of CO_2 in the air with which the blood is saturated. The total pressure or tension of the gases in air at average sea level barometric pressure is 760 mm. of mercury. If dry air contains 5 per cent of CO_2 the tension of CO_2 is 0.05 of 760 or 38 millimeters. When blood plasma is saturated at body temperature with pure CO_2 at 760 mm. tension, the plasma dissolves 51 volumes per cent of CO_2 as free carbonic acid, which is symbolized as H_2CO_3. If the CO_2 tension of the saturating gas is 40 mm., as it ordinarily averages in the alveolar air, the plasma H_2CO_3 content is

$\frac{40}{760} \times 51 = 2.7$ c.c. per 100 c.c. of plasma, or 2.7 volumes per cent as ordinarily expressed. The free carbonic acid content, H_2CO_3, of the blood is therefore dependent on the CO_2 tension of the air with which the blood is saturated.

In the case of arterial blood, this air is that of the pulmonary alveoli. If one breathes more deeply and rapidly than usual the CO_2 of the alveolar air becomes more diluted; in other words its tension falls, and the H_2CO_3 of the blood falls proportionally. The point which represents the condition of the blood on the CO_2 absorption curve of Fig. 1 then moves from its normal place, corresponding to about 40 mm. of CO_2 tension, to a place further to the left. As the result of the decrease in H_2CO_3 the $BHCO_3$ content of the blood becomes lower, some of the base being changed from bicarbonate to the form of alkali hemoglobinate, BHb. Such a change is merely a respiratory one, and does not indicate any change in the supply of available buffer alkali. A decrease in the alkali reserve, such as would be caused by addition of lactic or hydrochloric acid to the blood, would be shown by a fall in the level of the entire CO_2 absorption curve. That is, with a normal CO_2 tension the amount of base free to form bicarbonate would be decreased. In general, *acid-base changes due to respiratory retention or blowing off of CO_2 are shown by movements back and forth on the CO_2 absorption curve, while changes due to loss or retention of non-volatile acids, or of alkali, are shown by rise or fall of the level of the entire curve.*

The slanting straight lines drawn from the origin across Fig. 1 represent pH values calculated by the Henderson-Hasselbalch equation. They enable one to visualize the manner in which the blood pH changes in conditions of CO_2 excess and deficit, and of alkali excess and deficit.

A somewhat more convenient way of charting the CO_2 absorption curve was introduced by J. P. Peters (39), and is shown in Fig. 2. It is the same as Fig. 1, except that the CO_2 tension and CO_2 content values are laid off in logarith-

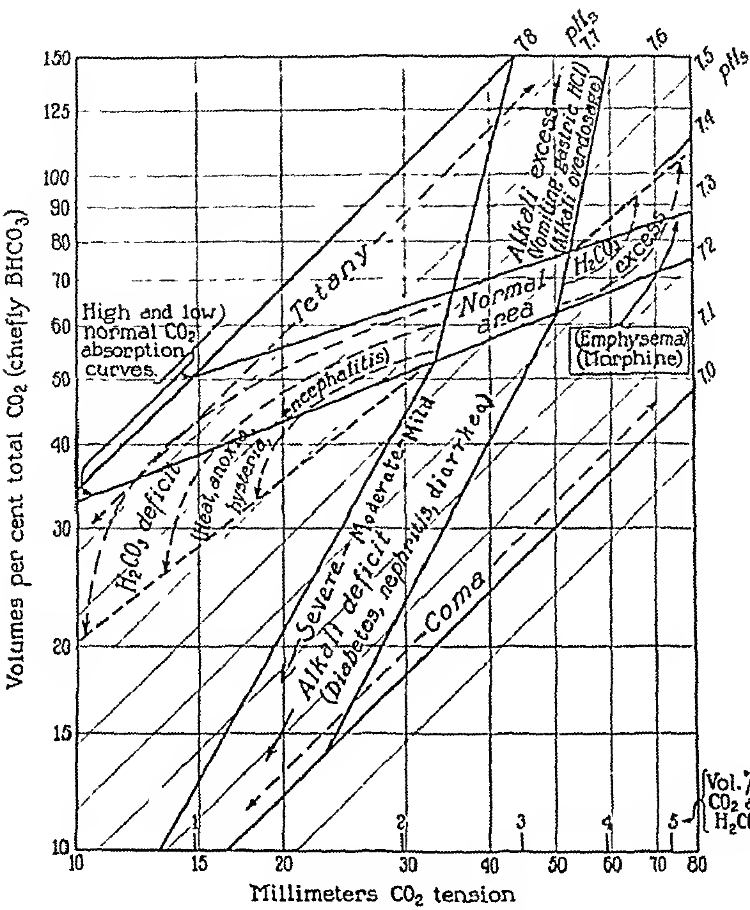

Fig. 2. Changes in CO_2 content, H_2CO_3 content, CO_2 tension, and pH of the blood plasma in conditions of carbonic acid excess and deficit, and of alkali excess and deficit. A point located in the wedge-shaped area between two fields indicates a mixture of the conditions indicated by the adjacent fields.

mic scales, the intervals denoting 1 volume per cent of CO_2 content or 1 mm. of CO_2 tension becoming greater for lower CO_2 values. The convenience of this form of chart is that the pH lines become parallel, and the CO_2 absorption curves, above 10 mm. of CO_2 tension, become nearly straight lines. We shall use this chart to illustrate the changes that occur in conditions of H_2CO_3 excess and deficit, and of alkali excess and deficit.

The chart expresses values of the plasma centrifuged from the blood, rather than of the whole blood. The reason for preferring plasma values is that CO_2 content in the cells is only about 0.6 as great as in the plasma. Consequently, in a series of bloods which all have an identical average normal acid-base balance as indicated by plasma bicarbonate and pH, but in which the proportions of cells and plasma are different, the anemic bloods will show higher than average normal whole blood CO_2 contents, which might be interpreted to indicate alkali excess, while the polycythemic bloods will show the reverse.

Carbonic Acid Excess

Causes. This condition is of respiratory origin and is due to conditions which prevent a normally efficient aeration of the blood in the lungs. It occurs when anatomical changes in the lungs interfere with aeration of the pulmonary blood, or when the respiratory center is dulled, so that breathing is retarded.

Experimentally it can be produced by breathing air containing 4 or 5 per cent of CO_2, or simply by holding the breath, or by the mechanical interference of partial tracheal obstruction. It is also caused by morphine administration, which deadens the respiratory center.

Clinically the condition has been identified by Meakins (31) and Dautrebande (7) in emphysema and in conditions of bronchitis and asthma in which pulmonary gas exchange is interfered with. In asthma and bronchitis it is probable that passage of air into the alveoli is retarded by contraction of the bronchi and bronchioles, while in emphysema the retarding changes are presumably in the alveoli. In morphine poisoning carbonic acid excess occurs (21) and is attributable to deadening of the respiratory center. In Cheyne-Stokes breathing it occurs momentarily during the periods of apnea (1).

Effects of carbonic acid excess. The effect on the acid-base condition in the blood is indicated by the "H_2CO_3 Excess" area in Fig. 2. The point representing blood conditions is immediately displaced by CO_2 retention, and moves to the right along the CO_2 absorption curve of the particular blood in question. The direction of the movement is indicated by the arrows to the right of the normal area. There is an increase in the CO_2 tension and a decrease in the pH in this CO_2 acidosis. The alkali reserve is at first not affected, but after some hours of carbonic acid excess a compensatory increase in the alkali reserve sets in, shown by the upward curve of the arrows towards their points. This increase was demonstrated by Yandell Henderson and Haggard (21) in experiments on dogs, and was noted by Dautrebande in the emphysematous patients whom he examined. In such cases, in which the condition is chronic, the points indicating the blood condition are found near the tips of the arrows in this area on the chart, above the level of ordinary CO_2 absorption curves. The increase in alkali reserve is presumably caused by the increased urinary excretion of acid, in titratable form and as ammonium salts, which accompanies the H_2CO_3 excess.

The only subjective symptom attributable to the condition is the exertion dyspnea, which is seen in subjects such as emphysematous patients, in whom the H_2CO_3 retention is due to pulmonary mechanical interference. Such individuals do not, even while at rest, ventilate their lungs well enough to prevent some H_2CO_3 increase in the blood. And when CO_2 formation in the body is increased by exercise, the carbonic acid retention quickly increases. There is a maximum effort to blow off the retained carbon dioxide, but it is only partly successful, and the patient has the same feeling of distress that is produced by holding one's breath.

Clinically the condition of carbonic acid excess is not in itself serious. As will be seen from Fig. 2, the decrease in pH is slight, and after compensatory increase in alkali

reserve has occurred the H_2CO_3 retention may be quite balanced by the increased $BHCO_3$, so that the pH returns to normal. Much more important than the acid-base alteration in such cases is the oxygen lack that threatens the organism. As shown by the Danish physiologist, Krogh (23), oxygen diffuses many times more slowly than carbon dioxide through membranes. Consequently whenever there is CO_2 excess from pulmonary malformations or from deadened respiratory center, there is a still more marked oxygen deficit in the arterial blood (18). Emphysematous patients who have sufficient CO_2 retention to be dyspneic also as a rule have so much arterial anoxemia that they are cyanotic.

The amount of CO_2 acidosis that occurs will never damage the patient, but the anoxia may readily reach the same stage which at high altitudes causes distress even to normal subjects. The CO_2 retention, in fact, is probably beneficial in such cases, because the excess of H_2CO_3 and the consequent slight decrease in blood pH stimulate the respiration, and thereby cause the anoxia to be less severe than it would with a normal acid-base balance. Furthermore the dyspnea, which results in such patients from increased excess H_2CO_3 when they exercise, is doubtless a salutary check to prevent them from undertaking exertions for which their lungs can not supply the necessary oxygen.

Carbonic Acid Deficit

Causes. This condition results when ventilation is so stimulated that CO_2 tension in the alveolar air and the blood is reduced below the level required to maintain the usual pH in arterial blood. The $BHCO_3 : H_2CO_3$ ratio increases because the denominator becomes smaller, and in consequence the pH rises. The condition is one of respiratory alkalosis.

The respiration is as a rule so regulated that the alveolar and arterial CO_2 tensions and the pH are kept within the limits indicated by the normal area in Fig. 2. The lungs,

however, also serve other functions: they oxygenate the blood, and at times their assistance is needed in cooling the body. When need for either of these functions becomes great, that need partially usurps control of the respiratory rate, which is accelerated with a certain amount of disregard for maintenance of normal pH. In consequence the blood pH may rise so high, as indicated in Fig. 2, that tetany results.

Experimentally this condition can be readily produced, as in Grant and Goldman's work, simply by voluntary overbreathing for some minutes. Bazett (2) produced it to the point of tetany by immersing the body in a hot bath, so that ventilation of the lungs was the only channel for escape of bodily heat. To a lesser degree hyperventilation occurs in high altitudes, where the oxygen concentration of the air is diminished and increased respiration is needed to maintain oxygenation of the blood.

Clinically a mild degree of alkalosis from carbonic acid deficit has been noted in fevers due to various causes (Koehler [22]), and a more severe form has been observed in some cases of encephalitis, in which the condition may approach tetany (Harrop and Loeb [16]). In this disease it appears that the central nervous infection may cause a state of hyperirritability of the respiratory center. Nervous or hysterical individuals sometimes overbreathe merely as the result of excitement, and may continue until symptoms of tetany appear.

Effects of carbonic acid deficit. The first effect of such hyperpnea is to lower the CO_2 tension and in consequence raise the pH in the blood. The point representing in Fig. 2 the condition of the plasma moves to the left from the normal area. The height of the CO_2 absorption curve, and therefore the alkali reserve, are not changed for some time. However, as the apparent result of the increased pH of the blood, the acid excretion in the urine is replaced by alkali excretion and the alkali reserve of the blood begins a gradual fall. The point representing the acid-base

balance of the plasma then follows the downward curve of the arrows in the "H_2CO_3 deficit" area of Fig. 2. The effect of diminishing the alkali reserve is to decrease the $BHCO_3$ and lower the pH part way back towards normal. The diminution of the alkali reserve is regularly noted in men who go to high altitudes, and appears to reach a limit after a few days residence there. The fall in alkali reserve appears to be almost directly proportional to the fall in barometric pressure (8), and may be great enough to bring the bicarbonate content down to the region indicated by the broken line at the bottom of the CO_2 deficit area in Fig. 2.

Treatment of carbonic acid deficit. The most serious symptom that can be attributed to carbonic acid deficit is the tetany. The drug which has been found to quiet the respiratory center, and which should therefore serve to combat the condition, is morphine. Other sedatives appear not to have been investigated.

Alkali Excess

Causes. This condition can arise from either of two causes: (1) Alkali buffer salts may be absorbed, either as such ($NaHCO_3$, Na_2HPO_4), or as alkali organic salts (sodium acetate or citrate) of which the organic radicle is burned, forming bicarbonate in the body. (2) The body may lose acid, as by vomiting gastric HCl. In either case the effect is to increase the reserve of buffer alkali in the body, since the excess of base over strong acids automatically divides itself between bicarbonate and the other buffers.

Effects of alkali excess. The symptoms referable to the acid-base disturbance in both cases are similar. The blood bicarbonate and pH increase, and if the condition goes far enough tetany of alkalosis may occur. The history is usually sufficient to indicate whether the condition is due to alkali dosage or to loss of gastric HCl. Also, when it is due to retention of alkali salts, the excretion of bicarbonate in the urine may be several grams per hour. Whereas if loss of

gastric juice is the cause there is so great a loss of salts from the body that the bicarbonate is held back by the kidneys in the apparent attempt to preserve the total salt content of the body fluids. The urine in alkalosis caused by loss of gastric HCl is usually alkaline and contains some bicarbonate, but in smaller amounts than those excreted after alkali overdosage; and the urine may even remain acid (17). There is also as a rule a marked dehydration of the body when the alkalosis is due to loss of gastric juice, because sodium chloride and water are lost with the HCl, whereas retention of administered alkali is likely to be accompanied by water retention rather than by dehydration.

The effects of alkali excess on the urine are usually to make it alkaline, diminish the ammonia to almost zero, and cause excretion of bicarbonate, which in amount is dependent on the origin of the condition, as indicated above. The sum of ammonia and titratable acid in the urine usually approaches zero when the plasma CO_2 rises to 75 or 80 volumes per cent.

Treatment of alkali excess. When the condition is due to administration of alkali salts no treatment appears to be necessary. The kidneys excrete bicarbonate and retain acid radicles, and rapidly restore the blood to normal condition.

When the alkali excess is caused by loss of gastric HCl, such as occurs in toxic vomiting and pyloric or intestinal obstruction, the treatment found efficacious has been administration of salt and water (11). The absorbed saline solution corrects the dehydration, which is probably the most serious factor in this condition, and as soon as the total salt content of the body fluid has been restored the kidneys excrete the excess of bicarbonate and restore the acid-base condition to normality. Administration of acid or acidifying salts does not appear to be necessary.

Alkali Deficit

This is the acid-base abnormality which is of the most clinical importance, and we shall therefore discuss it somewhat more fully than the foregoing types. It is the condition encountered in the acidoses of diabetes, of diarrhea and of nephritis.

Causes

Alkali deficit can arise from either of two causes: (1) Alkali may be lost from the body in the form of bicarbonate, which is the only form in which significant amounts of base appear to leave the body without equivalent amounts of fixed acids. (2) Non-volatile acids, such as lactic, hydroxybutyric, or hydrochloric, may be retained in the body, and exhaust equivalent amounts of buffer alkali. Either of these causes is capable of producing severe acidosis of the alkali deficit type.

1. *Loss of alkali bicarbonate from the body.* In severe diarrhea it appears that large amounts of alkali bicarbonate can leave the body by way of the intestine. Gamble and McIver (10) have shown that the salts of bile and pancreatic juice consist chiefly of alkali bicarbonate. It appears probable that loss of this bicarbonate is the cause of the acidoses that occur in the diarrheas of infants, and of cholera in adults (Peters and Van Slyke, p. 980 [40]).

Theoretically, it should be possible to produce a similar loss by a combination of achylia gastrica and intestinal obstruction so located that bile and pancreatic juice would be vomited. Actually, however, it does not appear that alkali deficit from this cause has ever been observed, nor as yet produced experimentally. In the cases of intestinal obstruction and fistula reviewed by Walters, Kilgore and Bollman (51) the loss of gastric HCl has been more important than the loss of alkaline secretions from the intestinal juice. The result has been, not alkali deficit, but alkali excess in the blood, such as we have noted in connection with loss of gastric HCl in pyloric obstruction. The only difference observed has been that the alkali excess

appears to develop less rapidly as the obstruction or fistula is farther down the intestine.

The kidneys excrete significant amounts of bicarbonate only when there is a state of alkalosis, due either to alkali excess or to carbonic acid deficit, two conditions which we have already discussed. When the acidosis of alkali deficit occurs, the urine becomes acid, alkali excretion stops and is replaced by excretion of acid in the form of ammonium salts and titratable acid. Urinary loss of alkali may be excluded as a cause of internal alkali deficit..

The one important path of alkali loss from the body appears to be by way of diarrheal discharges.

2. *Retention of fixed acids.* (The term "fixed acids" is used to indicate acids other than carbonic.) This is the most frequent cause of alkali deficit in adults. For example, the lactic acid acidosis of exercise, the acidoses produced by retention of phosphoric and sulfuric acids in nephritis and by retention of ketone acids in diabetes, and in the explosive ketoses of children. In each of these cases some endogenous acid is formed more rapidly than it is removed by chemical destruction or excretion. Hence the name *acidosis* was originally applied to states of alkali deficit.

Experimentally, alkali deficit from acid retention can be produced by severe exercise or anoxia (lactic acid retention), by administration of mineral acids, as in Walter's experiments, or by oral administration of ammonium, calcium, magnesium, or strontium chloride. The ability of these "acidifying salts" to lower the alkali reserve was discovered by J. B. S. Haldane (12, 13). The ammonia salts are absorbed, and the ammonia is changed to urea, setting free the HCl of the NH_4Cl. Ammonium sulfate and nitrate act similarly. When the Ca, Mg, or Sr chloride is given, the cation is excreted from the intestine and the HCl retained. Because of the diuretic effect of acid retention, these salts may be used as diuretics in conditions where some loss of alkali reserve can be tolerated.

Effects of Alkali Deficit

In the blood the bicarbonate content and pH are at once lowered, as the result of decomposition of $BHCO_3$ by the invading acid (See Fig. 2).

Respiration accelerates, so that the CO_2 formed from the decomposed bicarbonate is blown off, and hyperpnea then continues at a sufficient rate to keep the H_2CO_3 content of the blood lower than normal, so that the pH does not remain so low as it would have been without this hyperpnea. The respiratory acceleration is, however, not so great relatively as the fall in blood $BHCO_3$; if it were, the $BHCO_3:H_2CO_3$ ratio and hence the pH would remain entirely normal. For example, if CO_2 in the form of plasma $BHCO_3$ fell from 60 to 30 volumes per cent, and respiration doubled so that the CO_2 tension also fell to half (from 40 to 20 mm.) it is apparent from Fig. 2 that pH would remain constant at 7.42. On the other hand, if there were no respiratory acceleration at all, CO_2 tension would remain at 40 mm., and pH would fall to 7.1. What ordinarily happens, as indicated by the path of change on the diagram, is a compromise. There would be, in the example cited, enough hyperpnea to lower the CO_2 tension to about 30 millimeters, so that the pH falls only to about 7.25 instead of 7.10. Respiration would then remain at about 1/3 above the normal resting rate, e.g., raised from 5 liters per minute to 7 or 8. At this level the respiration would be maintained, apparently by the effect of the increased hydrion concentration of the blood on the respiratory center (15, 52).

There are, as we have shown, other factors, such as heat, outside of the acid-base balance which affect respiration, but the acid-base factor in the blood which under ordinary conditions has chief control appears to be the pH.

It is true that H_2CO_3 excess also causes hyperpnea, but the stimulant appears to be the increased hydrion activity. If it were the H_2CO_3 we should not have the picture seen here in alkali deficit, where there is hyperpnea with *less than normal CO_2 tension and H_2CO_3 concentration.*

In extreme alkali deficit, when the plasma pH is lowered to 7 or below, the hyperpnea may be the most striking feature of the entire clinical picture. Respiration may reach its mechanical limit, with the fearful air-hunger described by Kussmaul.

The circulation responds with an increased pulse rate. Tachycardia was one of the effects first noted in Walter's classic experiments.

On *renal excretion* the effect varies according to the cause of the alkali deficit.

When the cause is retention of fixed acids, such as the ketone acids in diabetes, or of HCl or other mineral acids given by mouth as free acids or as calcium or ammonium salts, the kidneys react with an elimination of the invading acid in the form of its alkali salts produced by decomposition of body bicarbonate. If the acidosis continues and the supply of buffer alkali decreases, ammonia formation by the kidneys greatly accelerates, and increasing amounts of the invading acid are eliminated as ammonium salts. With the salts of the foreign acid the kidneys, with apparent temporary loss of discrimination, excrete some of the body's supply of sodium chloride. With the salts goes an equivalent volume of the body fluid. Acidosis of this type therefore has a powerful diuretic effect, and results in dehydration of the body from loss of its saline fluids. This dehydration in diabetic acidosis may be so great that it contributes seriously to the state of collapse.

When the cause of the alkali deficit is alkali loss in diarrheic stools, the effect on the urine is not diuresis but oliguria. The salt and water loss through the intestine is so great and produces such rapid desiccation of the body that the diuretic influence of the acidosis is quite overcome. The urine volume may become so small that retention of nitrogen occurs, and symptoms of uremia.

After one or more days of severe alkali deficit, either from acid retention or from alkali loss, there is usually a

dehydration of the body. If body saline fluids have not been lost through the intestine they have been wasted through the kidneys. For this reason, *treatment of severe alkali deficit usually calls for administration of salt and water to replace fluid loss as well as of alkali to restore the alkali reserve.*

Defense Reactions of the Organism Against Alkali Deficit

These reactions appear generally to rank as follows with regard to the rapidity with which they begin effective work against the threatened acidification of the body.

1. The *buffers* of the body neutralize the invading acid. This reaction is instantaneous, as soon as the acid comes into contact with the buffers in the blood and the tissues. As we have stated, it is estimated that in an adult man the blood contains enough buffers, as alkali bicarbonate and hemoglobinate, to neutralize about 150 c.c. of N/1 acid, and the rest of the body enough additional buffers to bring the total tolerance of invading acid up to about 1 liter of N/1 acid.

2. The *lungs* drive off the CO_2 that has been formed by decomposition of body bicarbonate. They furthermore increase their ventilation rate, so that not only the newly formed H_2CO_3 is removed, but also part of the pre-existing H_2CO_3. In consequence, as we have shown, the $BHCO_3:H_2CO_3$ ratio and the pH do not fall so far as they would if the $BHCO_3$ were lowered while the H_2CO_3 remained constant (Fig. 2).

3. The *kidneys* begin to excrete acid phosphate, and in diabetic acidosis, free hydroxybutyric acid. They thereby diminish the acid retention. Later the kidneys begin to excrete more than usual amounts of ammonia, and if the acidosis continues ammonia formation becomes the chief defense against it.

Excretion of acid phosphates sets in at once, and assists in combating the loss of alkali reserve. J. B. S. Haldane (14) showed that the excreted phosphoric acid is in part at least derived from the organic phosphoric esters of the blood, which greatly diminish during the first days of experimental acidosis.

With continuance of the acid invasion, the phosphate excretion becomes retarded, apparently because of exhaustion of the supply of organic phosphates, and *ammonia excretion* becomes important. In quickly induced experimental acidosis ammonia excretion may be very little accelerated during the first day, even though the blood bicarbonate falls to less than half the normal value and the pH to 7.1-7.2 (Følling, 9). It is only later, after the supply of readily excretable base and phosphate is diminished, that ammonia formation greatly increases. (When the acidosis is caused by administration of acid phosphate Marriott and Howland (30) showed that no increased ammonia output occurs.) The excreted ammonia, as shown by Nash and Benedict (33), is formed in the kidneys. It enables the body to eliminate the invading acid as its ammonium salt, and to spare the alkali reserve. The end results of the procedure may be represented by the reaction:

NH_4HCO_3	+	NaA	=	NH_4A	+	$NaHCO_3$
formed from urea in kidney		salt of invading acid		excreted		retained in blood

If the kidneys are diseased ammonia formation may fail to increase. Consequently, as shown by Rabinowitch (41), there is more danger of acid intoxication in diabetes if nephritis is also present. In severe nephritis ammonia formation diminishes (35, 47). Even if acidosis is present the ammonia output may be less than the usual normal.

In diabetic acidosis it happens that the chief invading acid, *hydroxybutyric*, is such a weak organic acid that at the most acid reaction of the urine, about pH 5, nearly half of this *acid can be excreted in the free form,* with-

out neutralization by ammonia or body alkali. In no other type of clinical alkali deficit, however, does it appear that the invading acid is weak enough to be excreted to an important extent in the free form. The organism must rely upon ammonia formation to restore its alkali reserve.

Even in diabetic acidosis, ammonia formation is ordinarily the chief means by which the invading acid is prepared for excretion. In severe cases the ammonia excretion in 24 hours may be equivalent to 600 c.c. of N/1 solution, while the maximum free acid output is only about ¼ as much.

4. When the invading acid is organic, *combustion* may remove it as soon as conditions permit. In diabetic acidosis combustion can be accelerated by administration of insulin and glucose. In the lactic acid retention following severe exercise or intense anoxia combustion occurs quickly when the muscles rest or the blood is again adequately oxygenated.

Treatment of Alkali Deficit

When the plasma CO_2 is below 50 volumes per cent, with decreased or normal pH, there is alkali deficit, but it is too mild as a rule to require alkali therapy unless the CO_2 is below 40 volumes per cent (45). Obvious symptoms, such as hyperpnea and drowsiness, are usually not marked until the CO_2 falls below 30. When this point is reached the condition may be considered severe, and therapy is usually advisable.

The general therapy for alkali deficit remains alkali administration, as recommended fifty years ago by Stadelmann. But experience has shown fluid loss to accompany alkali deficit so frequently that administration of sodium chloride and water is almost regularly required with the alkali therapy. The administration is preferably oral when the alimentary tract will absorb it and the need is not urgent. But in severe diabetic acidosis the need may be urgent, and in the severe diarrheas of cholera and of infants

there is both urgency and intestinal intolerance. Intravenous injection is then indicated, at least for the first treatments.

By mouth alkali may be given in the form of bicarbonate, citrate, or acetate of sodium. The organic radicles of the citrate and acetate are burned, so in the body these salts are turned into bicarbonate.

For intravenous injection, sodium bicarbonate alone has thus far been ordinarily used. An isotonic solution of it contains 13 grams per liter. If the solution is first prepared and then sterilized by heat, it turns intensely alkaline from loss of CO_2, and the reaction must be restored by running a stream of carbon dioxide through the solution until it is no longer red to phenolphthalein. However, a more convenient way was introduced by Rogers (42), who sterilized the solid bicarbonate by dry heat in packages, and then dissolved it in sterile water or saline solution.

The amount of bicarbonate required to restore a normal alkali reserve can be calculated from the CO_2 content of the blood plasma (Palmer and Van Slyke [38]). The rises in plasma CO_2 and bicarbonate concentrations are approximately what they would be if the bicarbonate were added to a volume of fluid containing 0.7 liter for each kilo of body weight. The amounts required to raise the alkaline reserve to the point indicated by 60 volumes per cent of plasma CO_2 content, or 25 millimoles of $BHCO_3$, and pH 7.4 are indicated by the line chart on Fig. 3.

When injections are given it is well to calculate both the amount of bicarbonate required to restore a normal alkaline reserve and the volume of fluid required to restore that lost from the body, as nearly as this can be estimated from the loss in body weight or otherwise. To the volume of isotonic bicarbonate solution required to restore the alkali reserve is added the volume of 0.9 per cent NaCl solution required to make a total volume sufficient to replace the lost body fluids. When large amounts are required, the infusion is made in portions at suitable time intervals apart.

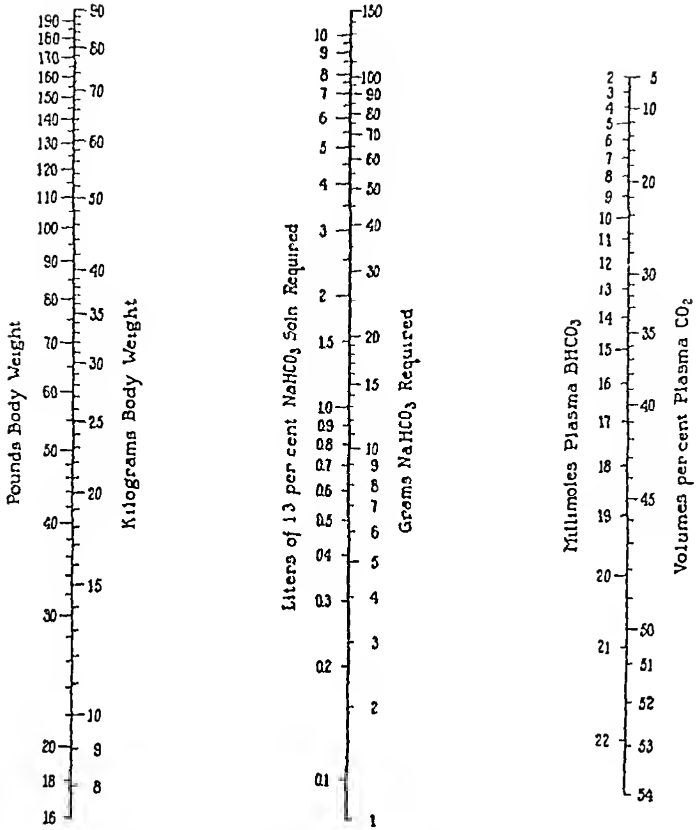

Fig. 3. Line chart for estimating the amount of sodium bicarbonate required in conditions of alkali deficit to raise the CO_2 content of the plasma to 60 volumes per cent or the $BHCO_3$ content to 25 millimoles per liter. A straight line cutting the scales for body weight and plasma CO_2 or $BHCO_3$ content will cut the middle scale at a point indicating the bicarbonate administration required.

The efficacy of such treatment in a condition complicated by extreme loss of both alkali and fluid is indicated by the results of Rogers (42) with Asiatic cholera; the mortality of severe cases treated with infusions of bicarbonate and salt was only one-fourth the mortality of similar cases not so treated. Rogers added 0.5 gm. of calcium chloride (presumably $CaCl_2.6\ H_2O$) per liter to his $NaHCO_3$-$NaCl$ infusions. The Ca concentration was about 2.5 millimolar, the same as in normal plasma. Cal-

cium addition seems logical in treating alkali deficit caused by diarrhea, because there is likely to be also calcium deficit, due to losses in the stools.

When severe acidosis was first noticed as a complication of the diarrheas of infants about 20 years ago, and bicarbonate therapy for the condition was introduced, the usual result was relief of dyspnea and temporary improvement, but death nevertheless. At that time the importance of treating also the dehydration factor was not realized. Salt was not given with the bicarbonate, and the bicarbonate itself was given in concentrations of 4 or 5 per cent: that is, with only one-third enough water to make an isotonic solution. Since then, however, Marriott, Schloss, and other pediatrists have pointed out the necessity of restoring lost salt and water, as well as alkali, and more cases are saved.

In the *acidosis of severe nephritis* alkali therapy may for a few hours restore a comatose patient to consciousness, but it is impossible to eliminate the retained and continually forming acid products, and it appears doubtful that the treatment prolongs life to a significant extent. It may, however, afford relief from the air hunger. In some cases dehydration and depletion of body NaCl are such that benefit is gained by saline infusions, but in other cases nephritic edema or cardiac edema is present to contraindicate saline treatment.

Special treatment of diabetic acidosis. In the days before insulin the treatment of a severe diabetic acidosis was an art demanding high skill and only to a certain extent definable by rules. The technique developed by Dr. Edgar Stillman (45) approached, I believe, the limit of success that was then attainable. Bicarbonate was given slowly by mouth, at the rate of about 3 grams per hour. Abundant fluids, with some salt, were given to obtain a free flow of urine and correct dehydration. Food was administered as it could be tolerated. The conditions of shock, chill, and dehydration, as well as the acidosis had to be combatted, and the patient so managed that the fluids and food given did not cause nausea, which might nullify the results of

hours of treatment. Acids were sometimes formed almost as rapidly as bicarbonate could be taken, so that 40 or 50 grams of bicarbonate on each of several successive days had to be given. In such cases the freshly formed acids made the eventual alkali administration much greater than that calculated from the plasma CO_2 at the beginning. The changes in alkali reserve had to be followed by repeated blood analyses. It sometimes required as much as 36 hours of minute attention to bring a patient back from the verge of coma, and several days to approach a normal alkali reserve, but Stillman proved that it could be done even in severe cases.

With insulin the problem is greatly simplified, and you have heard the technique of combined administration of insulin, glucose, and saline solution discussed so frequently that there is nothing to be added. The point that still remains somewhat under debate is whether in severe cases it is still advisable as a rule to give bicarbonate, or whether it is preferable to wait for the combustion of the ketone acids to restore the alkali reserve.

There appears, however, to be a definite advantage, and no significant disadvantage, in retaining the assistance of alkali therapy. Even when with insulin it is possible to restore the comatose patient without alkali, it can be done quicker if the latter also is used. Campbell, a member of the Toronto group which worked out the technique of insulin therapy, is of the opinion that as quick a recovery as possible from the state of deep acidosis is desirable in order to minimize the damage which the patient accumulates from remaining in that state (4). He believes that administration of sodium bicarbonate with the insulin-glucose treatment is desirable because it accelerates the recovery. When the absorbed bicarbonate is added to that formed in the body by combustion of sodium oxybutyrate, a temporary alkali excess may result later, as shown by Cullen and Jonas (6), but apparently the alkalosis is never serious. Campbell's combination of the pre-insulin technique of alkali therapy with the modern insulin treatment appears to be well founded.

Dietary prevention of diabetic acidosis. The 4-carbon acids, hydroxybutyric and acetoacetic, are formed in the body whenever fats burn without simultaneous combustion of a sufficient amount of carbohydrate. The long fatty acid chains can be burned down to 4 carbons each, even in total diabetes when no glucose at all is burned, but further combustion of the 4-carbon oxy-acids does not occur unless accompanied by glucose oxidation. The prevention of ketosis from accumulation of these acids in diabetes becomes the problem of ascertaining how much glucose must be burned to effect combustion of the 4-carbon acids from a gram of fat, and of regulating the diet accordingly.

The first quantitative data were obtained in 1914 by Zeller (54) in experiments on normal men. He found that with one gram of carbohydrate the body could burn about 4 grams of fat without forming more than small amounts of the 4-carbon acids.

Ladd and Palmer (25, 26) later showed that diabetics also can burn fats with about one-fourth the weight of carbohydrate. Ladd and Palmer furthermore pointed out that in practicable diets it is necessary to include in the total carbohydrate the 0.6 gram of glucose which Lusk had shown to be formed from each gram of catabolized protein. In order to obtain utilization of the greatest possible number of calories by a diabetic, therefore the fat intake could be calculated from the tolerated amount of carbohydrate and protein by the following formula,

$$\begin{aligned}\text{Fat} &= 4\ (\text{Carbohydrate} + 0.6\ \text{Protein})\\ &= 4\ \text{Carbohydrate} + 2.4\ \text{Protein}\end{aligned}$$

The quantities in the formula all refer to grams. The total caloric value for a diet so calculated is approximately 10 calories for each gram of fat. The formula indicates the combustion of approximately 2 molecules of fatty acid for 1 molecule of glucose. That diabetics could routinely ingest and burn such diets was shown by Ladd and Palmer, and independently by Woodyatt (53) and by Newburgh and Marsh (34).

Ladd and Palmer found that it was necessary to work up gradually to the full caloric intake, or severe ketosis might develop. The body requires some training on high fat diets before it develops its full fat-burning ability, expressed by the formula. Newburgh and Marsh (34) found that they could routinely start with 900 to 1000 calories and work up to 2000 or more, according to the caloric need and carbohydrate tolerance of the patient.

Woodyatt (53) and Shaffer (43) contributed much to the theory of the problem, and proposed formulae which included assumptions that the glycerine of the fat formed glucose, and that a certain amount of acetone bodies was formed from each gram of protein. However, it appears that all of the available quantitative knowledge obtained in experiments on man is expressed by the simpler formula of Ladd and Palmer.

With such a quantitative formula it became possible without insulin to construct diets of adequate caloric requirement for patients who would formerly have been kept in semi-starvation. And when insulin was given it was possible to minimize the amounts required.

NECESSITY OF DIAGNOSING ACID-BASE ABNORMALITIES BEFORE TREATMENT

Whenever regulation of the acid-base balance of the body is attempted, it should be preceded by a determination of the type and severity of the abnormality. And when an acute, rapidly changing condition, such as severe diabetic acidosis, must be handled, repeated analyses of the blood at intervals are needed in order to guide the treatment.

The methods for finding the state of the acid-base balance are now simple. The plasma bicarbonate can be determined by titration (49), or the total CO_2 content by a gasometric procedure (48) as simple as the hypobromite urea analysis. And the colorimetric plasma pH (5, 19) is hardly more difficult.

In the great majority of clinical cases the abnormality is one of alkali deficit or excess. As indicated by the paths of

these conditions in Fig. 2, plasma CO_2 or bicarbonate determination suffices for the diagnosis. Such is the case ordinarily in diabetes, nephritis, and diarrhea. Occasionally, when there is possibility of carbonic acid excess from obstructed or retarded pulmonary ventilation, or when there is possibility of carbonic acid deficit from overbreathing in fever, anoxia, or nervous conditions, it is essential to estimate also the pH. With the plasma pH and CO_2 content one can locate on a diagram such as Fig. 2 the point which indicates the nature of the acid-base change.

However, when laboratory facilities for blood analysis are not available, a simple test introduced by Palmer and Henderson (36) will often suffice to rule out alkali deficit. A slightly rounded teaspoonful of sodium bicarbonate (8-10 grams) is administered, and the urine is tested with litmus paper at half-hourly intervals for one or two hours. If the urine turns alkaline, alkali deficit can be excluded. If the urine remains acid, however, the acid-base balance may nevertheless be normal. If the alkaline reserve happens to be near the lower limit of normal, as much as 25 grams of bicarbonate may be required to turn the urine alkaline. Furthermore, in occasional pathological cases one may even give enough bicarbonate to produce an alkalosis, and the urine will still remain acid. The "bicarbonate tolerance" test is therefore valid only in one direction: if it turns the urine alkaline one may be certain that no acidosis exists. But if the urine remains acid a blood analysis must be done in order to ascertain the acid-base condition; there may or may not be an alkali deficit. A more sensitive improvement of the test has been devised by Palmer, Salvesen and Jackson (37), in which an increase of urine pH is looked for instead of development of a definitely alkaline reaction.

In a large proportion of cases in which acidosis is suspected the acid-base balance is normal, and in most such cases the urine will turn alkaline when the Palmer-Henderson alkali tolerance test is tried. Many blood analyses can therefore be dispensed with if a preliminary examination is made with this test.

Presence of even considerable amounts of acetone bodies in the urine does not necessarily indicate the existence of an internal acid deficit. I have seen a urine which turned almost black when tested with ferric chloride for aceto-acetic acid, and which in fact contained 20 grams of hydroxybutyric acid per liter, and yet the acid-base point of the blood plasma was within the normal area. The case was one of toxemia of pregnancy, with anorexia and vomiting. There was the same ketosis which hunger produces in normal subjects, but the 24-hour urine volume was only 400 c.c. so that, despite its concentration in hydroxybutyric acid, it represented only about 8 grams excretion per day. Production of this amount would not cause a serious fall in the alkali reserve. In this case the acidifying effect was entirely neutralized by loss of vomited gastric hydrochloric acid. What the patient needed was not treatment for acidosis, but restoration of body fluids by salt and water, with glucose to combat the effects of starvation.

An example will indicate the consequences that may follow treatment instituted and carried on without diagnosis of the acid-base balance in the blood. A number of years ago, it was somewhat the vogue to treat pneumonia with bicarbonate, with the idea that it would ease the rapid respiration and decrease its exhausting effect. One could expect this to be the case only if the cause of the hyperpnea were alkali deficit, which, as Hastings, Neill, Morgan and Binger (18) showed, seldom occurs in pneumonia. The hyperpnea has its origin in the pulmonary changes, and not in acidification of the blood. Nevertheless the alkali treatment was administered to many patients as a routine, and one of these was referred to Binger (3) in the Hospital of the Rockefeller Institute. The patient had been apparently convalescent for several weeks, and during this time had been receiving several grams of bicarbonate daily. Nevertheless she was becoming increasingly cyanotic and dyspneic. Examination of the blood showed a state, not of acidosis, but of alkali excess, attributable to the bicarbonate therapy. The patient also had a mild chronic nephritis, with a tendency to formation of edema. The

kidneys had not been excreting the excess of bicarbonate, which had been retained and had caused the development of edema. The cyanosis was due to pulmonary edema. Both edema and cyanosis disappeared in the course of some days after alkali excess had been diagnosed and the bicarbonate administration discontinued.

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DEHYDRATION AND MEDICAL SHOCK*

DANA W. ATCHLEY

In 1831 Dr. W. B. O'Shaughnessy of Newcastle-upon-Tyne wrote a brief letter to the London Medical Gazette which embodied the results of several years of what he termed his "experimental inquiries" into the cholera. His terse summary of a physiological mechanism in terms of what we choose to call modern chemistry is a delightful contrast to the usual clinical sophistry of that day, and perhaps this, and compels me to quote his communication *in toto.*

"1. The blood drawn in the worse cases of the cholera, is unchanged in its anatomical or globular structure.

2. It has lost a large proportion of its water. 1000 parts of cholera serum having but the average of 850 parts of water.

3. It has lost also a great proportion of its *neutral* saline ingredients.

4. Of the free alkali contained in healthy serum, not a particle is present in some cholera cases, and barely a trace in others.

5. Urea exists in the cases where suppression of urine has been a marked symptom.

6. All the salts deficient in the blood, especially the alkali or carbonate of soda, are present in large quantities in the peculiar white dejected matters."

I think you will agree with a contemporary reviewer of Dr. O'Shaughnessy's "Chemical Pathology of Cholera" who in the Lancet of 1832 called particular attention to

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Delivered October 26, 1933.

the "strictly logical series of deductions disfigured neither by empty hypothesis, nor by untenable and wild speculations." This same reviewer goes on to say: "This is what we want in medical reasoning. Let nothing be argued upon until it is proved; let no fact be received until its truth is established; then and not till then, will medicine rank as a science, and the disputes and cavillings of its professors become susceptible to adjustment according to exact and incontrovertible data."

Turning next to the therapeutic implications which naturally follow from the biochemical disturbances found to be present in the disease, Dr. O'Shaughnessy states that the cure is seemingly dependent upon two principles:—"First, to restore the blood to its natural specific gravity (i.e. its water content); second, to restore its deficient saline matters." He then states that, "the first of these can only be affected by absorption, by imbibition, or by the injection of aqueous fluid into the veins. The same remarks, with sufficiently obvious modifications, apply to the second." The practical application of these principles was described as follows: "In severer cases copious enemata of warm water, holding the natural salts of the blood in solution are strongly recommended. . . . When absorption is entirely suspended the author recommends the injection into the veins of tepid water holding a solution of the normal salts of the blood." Thus it is apparent that 101 years ago a physician with an investigative and critical mind was able, with the crude methods at his disposal, to unravel the mechanism of the essential manifestation of cholera, viz. dehydration, salt depletion and shock. Furthermore, he logically employed the specific therapy indicated by such a disturbance in physiology.

Although the implications of O'Shaughnessy's brilliant work were confirmed by a number of workers at home, as well as on the continent, the struggle to overcome the traditional prejudices of those in authority is beautifully exemplified by the following words written by Dr. J. Pidduck to the London Medical Gazette, August 21, 1832.

"Turning hopelessly away from the Central Board and Local Hospital, I resolved to pursue the experiment (i.e. saline therapy) among the poor in my district, convinced that the brandy and laudanum system had been too highly recommended, and too long sanctioned by authority, to admit of the introduction by the same individuals of another system so diametrically opposed to it. Perhaps such a revolution in a cherished opinion, and a favourite practice, would be a stretch of candour and liberality almost superhuman."

In spite of the fact that in 1850 the German biochemist Karl Schmidt confirmed and greatly amplified the analytical results of O'Shaughnessy there were subsequently but occasional references to the value of intravenous salt solution. It was not until Rogers, and Nichols and Andrews in 1909 used intravenous saline injections with remarkable decrease in mortality in a cholera epidemic in the Philippine Islands that this rational form of therapy became generally accepted. I have taken time to trace the development of the chemical pathology of cholera because it presents probably the earliest instance in which there was an understanding recognition of the physiological processes involved in the development of this common complication of many disease conditions, viz. dehydration, salt depletion and shock. Furthermore, it was in the treatment of cholera that, for the first time, a rational replacement therapy was instituted with, I might add, the anticipated clinical benefit.

Chronologically the next correct appraisal of the fundamental problem may be found in the Guy's Hospital reports of 1874. Dr. C. Hilton Fagge described, therein, "A Case of Diabetic Coma, treated with partial success by the injection of a saline solution into the blood." The most impressive feature of this pioneer experiment in therapy was the rationale which he offered. This is best expressed in his own words, "What suggested to my mind the advisability of injecting a saline solution into the blood in this case was the idea that coma was due to the drain

of water from the system, caused by the diabetes. I suppose that the hypothesis upon which I acted was essentially similar to that which formed the basis of the like treatment in the collapse of cholera." The importance of this observation was nine years later overshadowed by Stadelmann's discovery of the existence of an acidosis in diabetic coma. Stadelmann quite logically felt that the replacement of alkali was the obvious point of attack. This concept so completely dominated the treatment of diabetic coma that even the more modern text books omit mention of the clear correlation between dehydration and circulatory collapse which Fagge had demonstrated in 1874. One must not neglect to state that for at least twenty-five years salt solution has been routinely employed in the treatment of diabetic acidosis. However, it was believed that the picture of low blood pressure, thready pulse, oliguria and collapse resulted from "toxic" cardiac failure rather than from shock due to decreased circulating blood volume and vasomotor paralysis. In recent years it has been shown that the loss of salts and water in diabetes is dependent upon two unrelated mechanisms. One of these is the obvious loss of base resulting from the excretion of ketone acids. The other is definitely associated with the occurrence of severe glycosuria, and may be found even in the absence of ketosis, but the nature of its underlying physiological disturbance is not known.

The clinical picture dependent upon dehydration, salt loss and consequent shock is found in many other disease conditions. Prominent among these is the group characterized by pyloric or high intestinal obstruction, as well as those patients in whom for some reason there exist fistulous openings to the upper gastro-intestinal tract or the bile ducts. It naturally follows that the picture of shock in these patients results in part at least from constant vomiting or persistent drainage of body fluids normally rich in sodium salts. It should be pointed out that in certain cases of intestinal obstruction no actual loss of salt from the body occurs, but the same result is effected by the out-

pouring of salts and water into the distended loops of intestine, thus removing it from the circulating blood and tissue spaces. The chemical changes in the blood under these conditions, viz: decreased water, sodium and chloride content and increase in urea, have been recognized for many years. Furthermore, clinicians have for a long time appreciated the therapeutic value of intravenous salt solution. The original hypothesis assumed that the condition was due to a toxemia and that the saline therapy acted as a detoxicant. It remained for Gamble, about ten years ago, to show that for pyloric obstruction, at least, no other factors than salt loss and dehydration were to be found. In other words, as in cholera and diabetic acidosis, striking clinical improvement follows the replacement of salt and water.

Another situation in which shock plays a dominant role is found in the sequelae of severe burns. Of course, we recognize that there are probably several factors which may contribute to a fatal outcome, but certainly the one which today has greatest therapeutic possibilities is that resulting from dehydration and salt depletion. Serum exudation in the burned areas is an important component of the mechanism of this dehydration. The cause of the characteristic acidosis has been ascribed to the presence of certain unknown acids, but it may possibly be due to a loss of sodium and consequently a lowering of the blood bicarbonate. However, the nature of the complicated disturbances resulting from severe burns cannot be well understood without further chemical study.

The clinical syndrome of acute adrenal insufficiency as seen in Addison's disease bears a striking resemblance to that present in the other pathological states which I have discussed. For example, weakness, prostration, rapid pulse, nausea and vomiting, fall in blood pressure, decrease in water content of the blood, increase in blood urea and decrease in the concentration of chloride and bicarbonate are characteristic. We have shown that in adrenal insufficiency in man, the sodium of the blood is markedly

lowered, as Marine and Bauman and also Zwemer had shown in cats. Furthermore, we were able to show that the administration of sodium chloride alleviates to a striking degree the clinical manifestations just described. On the other hand, it is possible to precipitate an acute and alarming attack of adrenal insufficiency by the withdrawal of salt from the diet of patients who were in relatively good clinical condition as a result of salt therapy. It is truly remarkable to observe the difference that 15 grams of salt a day will effect in the health and well-being of such a patient. It has been demonstrated in our laboratories that the decrease in salt content of the blood in adrenalectomized dogs is due to an enormous increase in the excretion of sodium by the kidney. This loss of sodium is accompanied by an augmented but not parallel water output and results in the characteristic picture of dehydration, salt depletion and shock. It seems likely that the mechanism by which salt depletion and dehydration are produced in adrenal insufficiency is different from the disturbance resulting in shock in the clinical conditions described previously. On the basis of the evidence so far accumulated we are inclined to believe that the active principle of the adrenal cortex exerts a controlling influence upon sodium metabolism through the medium of the kidney, and that the breakdown of this regulatory mechanism results in an increased rate of sodium excretion. That the regulatory effect of the adrenal cortex upon salt and water metabolism is not its sole function is proven by the fact that adrenalectomized animals eventually succumb although the period of survival may be appreciably prolonged by salt administration.

It is apparent from the foregoing discussion that the loss of water and salt from the body may occur in a variety of ways and result from a number of different physiological disturbances. Among these we have described: loss of base and water by diarrhea, vomiting or surgical drainage; loss of serum by exudation in burns; loss of salt in the urine by alterations in the carbohydrate

metabolism; loss of salt as a response to acidosis; and finally, an excessive urinary excretion of sodium in adrenal insufficiency. It might be well to add the obvious statement that the simplest form of shock resulting from salt and water depletion is that due to acute hemorrhage. There is one common denominator to be found in all of these disease conditions, when they have reached an advanced state, viz. the shock syndrome.

I should like now to consider briefly the train of events by which dehydration and salt depletion ultimately lead to the classical syndrome of shock. One of the most striking physiological principles of the body is expressed in its tenacious effort to maintain the salt content of the blood serum and the interstitial fluids at a constant level in the face of amazingly adverse circumstances. Thus, when salt is lost for any reason, the body sacrifices its precious water stores to protect its sodium concentration. Conversely, the extensive loss of water is almost invariably associated with a considerable loss of salt. Now, severe drain of salt and water from the tissue spaces is reflected in the circulating blood, producing in time a decrease in blood volume so great that the state of shock ensues in much the same manner as in acute hemorrhage. Therefore, we are led to infer that the state of shock is the physiological result of an acute disparity between the circulating blood volume and the functioning capacity of the vascular bed. This may be brought about in one of two ways; either by a relatively rapid decrease in the circulating blood volume or by sudden expansion of the vascular bed. In the clearest example of the former, viz., acute hemorrhage, the decrease in blood volume is obvious, and the ensuing results have been adequately studied. In the other conditions which I have discussed, the mechanism is analogous to hemorrhage but there are many complicating factors still to be elucidated.

Let us now turn our attention to those situations in which the state of shock is brought about primarily by a rapid dilatation of the vascular bed rather than by con-

traction of the blood volume. Since the isolation of histamine by Sir Henry Dale in 1909, physiologists have recognized that large doses of this drug will cause a generalized capillary dilatation, drop in blood pressure and collapse. Of greater importance to the clinician is a discussion of those states in which this mechanism results from natural disease processes, rather than the artificial laboratory experiment. It was my privilege some years ago to observe the clinical effect of an intravenous rattlesnake bite. This patient while extracting venom at the American Museum of Natural History was bitten on the back of his hand. In spite of the immediate administration of anti-venom serum the patient collapsed in twenty minutes and was brought to the Presbyterian Hospital. On admission he presented an extraordinary picture. His skin was cold and dusky red in color, he was semi-comatose, his respirations were shallow, his pulse was rapid and almost imperceptible, his heart sounds were inaudible and his blood pressure was too low to be read. In spite of several saline infusions and a transfusion of 700 c.c. his blood pressure, which was raised by these therapeutic procedures soon fell to a critical level again. It was not until 7200 c.c. of fluids had been given intravenously in the course of sixteen hours that his blood pressure remained normal. The almost invariably fatal outcome from an intravenous rattlesnake bite results from failure to recognize the fact that the therapeutic attack should be primarily directed against the state of shock.

When Laennec in 1826 described the weakness of the heart sounds in severe febrile conditions, he attributed this change to cardiac failure, a point of view which, unfortunately, still continues to dominate medical thought. This is true in spite of the fact that Romberg and Pässler as early as 1899 wrote upon the effect of bacterial products on the vasomotor apparatus of rabbits. These authors were able to show that a state of collapse could be induced by the intravenous injection of pneumococci or other organisms. Furthermore, they pointed out that intra-

venous salt solution was more effective in treating these animals than was subcutaneous ether, camphor, strychnine or cognac. Romberg at that time suggested the term "toxic shock" for this complication of infectious disease. It is hardly necessary to emphasize the similarity between Romberg's "toxic shock" and the shock resulting from intravenous injections of histamine or snake venom.

A striking confirmation of the shock producing capacity of the pneumococcus was afforded by a clinical experiment performed upon himself by a member of our staff a few years ago. This individual gave himself a large dose of pneumococcus vaccine, intravenously. There followed an immediate and alarming collapse during which his systolic blood pressure fell to 60 mm. of Hg. and continued below normal for three days. In conjunction with this he developed numerous petechial hemorrhages of the skin, which would lead one to infer that in addition to dilatation there had also been actual capillary damage.

Doubtless you will all recall in your own experiences with severe infectious diseases, particularly pneumonia and typhoid fever, patients who have presented the picture of falling blood pressure, rapid pulse and collapse. Certainly, in many instances this serious complication is a manifestation of shock, and probably results from an increase in the vascular bed due to capillary damage. Confusion of this state with cardiac failure will result in misdirected and possibly harmful therapy. The importance of this point of view was pointed out by Theodore Janeway in the New York State Medical Journal for 1907, when he wrote on "Some Common Misconceptions in the Pathological Physiology of the Circulation and Their Practical Significance". He said: "We must in most cases abandon the idea of cardiac death at the height of acute infectious diseases such as pneumonia, typhoid fever and septic fevers. . . . In place of heart failure we must write vasomotor failure." The discussion of this complication of infectious disease in many modern text books of medicine offers a discouraging contrast to Dr. Janeway's enlightened attitude.

Up to this point, I have discussed the occurrence of shock in a variety of clinical conditions, stressing in each instance the mechanism which predominates the picture. In some of these situations shock resulted primarily from a rapid decrease in circulating blood volume, whereas in others the chief factor was vasodilatation. However, I think it is only fair to state that this is a diagrammatic visualization of processes which like other biological phenomena are more complex than I have seemed to indicate. For example, in histamine shock, although the primary disturbance is admittedly due to capillary dilatation, nevertheless capillary dilatation is almost inevitably accompanied by an increase in the size of the capillary pores which permits large quantities of blood serum to escape into the tissue spaces. Thus, the component of decreased circulating blood volume also plays a part. This effect may naturally be assumed to exist in the case of snake venom and bacterial capillary poisoning, or in any other condition in which generalized capillary dilatation is marked.

In diabetic acidosis accompanied by the shock syndrome, I have indicated the importance of dehydration and salt depletion. We have all seen patients in whom the state of shock has persisted after adequate replacement therapy and after the ketosis had disappeared. There is experimental evidence which suggests that there may be in these cases a factor of capillary poisoning which is responsible for the persistent recurrence of the shock syndrome. It has been shown that certain substances which have a chemical similarity to the ketone bodies, for example, acetyl acetone and sodium acetate, will produce vasodilatation in animals.

There has been much discussion of the participation of a toxin in the production of the clinical manifestations of intestinal obstruction and, indeed, substances with histamine-like action have been isolated from damaged loops of gut. To what extent these substances contribute to the total mechanism in producing shock is still problematical.

I have pointed out the role of dehydration and salt loss in severe burns but here, too, certain toxic substances are perhaps absorbed from the necrosing tissue and may act as capillary poisons.

It seems possible that there is still another mechanism involved in the production of shock through vasodilatation, though our understanding of the process is still obscure. I am referring to the influence of the sympathetic nervous system. This is dramatically demonstrated in the production of traumatic shock. Although severe and extensive traumatization of tissue results in a certain amount of dehydration by serous exudation and hemorrhage, it has been reported that injury to a limb isolated from the rest of the body except for its nerve supply may result in shock. Thus it would appear possible to induce shock without the aid of salt loss, dehydration or circulating toxin. In the field of internal medicine, it is recognized that one of the immediate effects of extensive infarction of the myocardium is a clinical picture of falling blood pressure and collapse, which is similar to, if not identical with shock. It is hard to believe that such a rapidly developing syndrome could result from tissue damage and it seems likely that it is brought about through a reflex nervous mechanism. Obviously, the development of shock in cardiac infarction is a fortunate physiological disturbance and hence should not be treated as in other conditions.

Before proceeding to the discussion of therapy, I should like to enumerate briefly a few of the systemic effects of shock. The most significant effect is the interference with tissue function which results from circulatory stasis and diminished blood supply. No organ shows this disturbance more strikingly than does the kidney. Renal function is compromised and anuria frequently results. This, in turn, definitely upsets the acid-base equilibrium of the body and in the case of diabetic shock prevents the excretion of ketone bodies, thus adding to the seriousness of the disease state. The tissues of the central nervous system are also

included in the general damage and the resulting pathology doubtless plays a large part in the terminal stages.

The treatment of shock is more or less independent of its cause. Whether it be due to trauma, toxemia, hemorrhage or dehydration, the physiological problem is the same; namely, a disparity between the circulating blood volume and the vascular bed. On one hand there is primarily a decreased blood volume from hemorrhage or fluid loss; on the other, an increased vascular bed resulting from capillary dilatation. The need for immediate measures to increase the circulating blood volume is common to all types.

I think it is fair to say that the longer the state of shock is permitted to exist, the more difficult it becomes to alleviate it and the higher is the mortality. Consequently, delay in initiating therapy is dangerous. As an emergency method, the intravenous injection of 50 c.c. of 50 per cent glucose, which may be conveniently kept on hand, is of some temporary value, as it will draw fluid into the blood stream from the tissue spaces. Its action is fleeting and it should be followed promptly by the intravenous injecton of 1000 to 2000 c.c. of normal salt solution. This procedure may be repeated within two or three hours without any danger to the myocardium. The response of the blood pressure is the best indication for such repetition. The value of salt solution in the treatment of shock developing in the course of infectious diseases has not been thoroughly tested, and final conclusions as to its usefulness are still uncertain. In shock due to other causes, dramatic results follow this therapeutic measure.

The ideal treatment for shock is a large blood transfusion, and every patient likely to develop shock should have his blood grouped early in the course of his disease. When salt solution fails, transfusion may turn the tide. The theoretical basis for the fact that blood is more effective than salt solution lies in the assumption that it contains a nondiffusible substance, i.e., serum protein, which

makes the influence of added blood a more permanent one. One cannot accept this suggestion without caution, for it has been clearly proved that in histamine shock whole serum leaves the blood stream; in other words, the capillaries become readily permeable to protein. However, there is no denying the greater therapeutic value of blood over all other fluids. In an attempt to find a substitute for blood, numerous colloidal substances have been tried. The most prominent of these is acacia. During the World War, this solution was tried and given up because of the severe reactions which frequently followed its administration. In the past two or three years, methods of preparation of acacia solutions have been improved, and while enthusiastic reports from its action have appeared, it is too early to recommend its general use.

It is obvious that all therapy in shock should be intravenous rather than subcutaneous or intramuscular. The rapidity of response is much greater when the intravenous route of administration is employed, because the poor peripheral circulation slows subcutaneous absorption tremendously. This applies to hypodermic medication as well as to fluid administration.

The use of vasoconstrictors, such as epinephrine, is not helpful and may, indeed, be dangerous. From a physiologic standpoint they are contraindicated because the blood vessels which they affect are already constricted to the disadvantage of the capillary circulation, as has been shown by studies of both the skin and visceral arterioles. There has been much mention of heat loss as a contributing cause of shock and it is consequently essential to keep the patient as warm as possible.

In conclusion I should like to say that while most of what I have had to tell you this evening is an old story, I feel that it is a story worth retelling because there is no doubt that the importance of the state of shock, particularly as it occurs in the field of internal medicine, has not received its just and proper emphasis.

PROCEEDINGS OF ACADEMY MEETINGS

FEBRUARY

STATED MEETINGS

Program arranged in coöperation with the SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE—February 1

I. EXECUTIVE SESSION—a. Reading of the Minutes; b. Election of Fellows and Members.

II. PAPERS OF THE EVENING—*Symposium: present status of the rheumatic fever problem*—a. Certain aspects of the pathology of rheumatic fever, W. C. Von Glahn; b. Clinical history of rheumatic fever and observations relating to etiology, T. Duckett Jones, Boston; c. Current conceptions of the nature of the disease, Homer F. Swift; d. Discussion, Louis Gross, John Paul, New Haven, A. Dochez, John Wyckoff.

THE HARVEY SOCIETY (IN AFFILIATION WITH THE NEW YORK ACADEMY OF MEDICINE) February 15

THE FIFTH HARVEY LECTURE, "The Clinical Application of Some Recent Knowledge of the Biliary Tract and of the Pancreas," Evarts A. Graham, Professor of Surgery, Washington University School of Medicine, St. Louis.

SECTION MEETINGS

SECTION OF SURGERY—February 2

I. PRESENTATION OF CASES—a. 1. Traumatic rupture of the common hepatic duct—2½ year result—2. Embryonal carcinoma of the testicle; orchidectomy with high ligation of the cord; deep X-ray therapy; 6 year result—3. Recurrent dislocation of the shoulder; Nicola operation; 2 year result, Kenneth M. Lewis; b. 1. Second acute perforation of marginal ulcer—2. Mikulicz operation on jejunum, Edward Victor Denneen.

II. PAPERS OF THE EVENING—a. The liver function test in cholecystectomy, Condict W. Culter; b. Acute cholecystitis. A study of 75 proven cases with subsiding or subsided clinical manifestations at time of operation, Arthur S. W. Touroff.

III. GENERAL DISCUSSION—Seward Erdman, Joshua E. Sweet, Frederic W. Bancroft.

IV. EXECUTIVE SESSION.

SECTION OF DERMATOLOGY AND SYPHILOLOGY—February 6

I. PRESENTATION OF CASES—From The Mount Sinai Hospital.

II. PRESENTATION OF MISCELLANEOUS CASES.

III. DISCUSSION OF SELECTED CASES. IV. EXECUTIVE SESSION.

JOINT MEETING—SECTION OF NEUROLOGY AND PSYCHIATRY *and the* SECTION OF MEDICINE—February 13

I. PAPER OF THE EVENING—The psychogenic origin of organic disease, Eli Moschcowitz.

II. ILLUSTRATIVE CASE PRESENTATIONS—a. From Mount Sinai Hospital, B. S. Oppenheimer, Solomon Silver (by invitation); b. From Presbyterian Hospital, George Draper; c. From New York Hospital, Ephraim Shaw (by invitation), George W. Henry (by invitation). III. GENERAL DISCUSSION.

SECTION OF ORTHOPEDIC SURGERY—February 16

I. PRESENTATION OF CASES—a. 1. A case presenting fracture of lumbar spine, os calcis, and carpal scaphoid, Martin W. Ware—2. Fracture of fibula—adhesive plaster dressing and immediate weight-bearing, Arthur Krida; b. 1. Fracture dislocation of elbow with resection—end result—2. Fracture and complete dislocation of lumbar vertebrae, Richmond Stephens, Raymond Lewis; c. Dislocation of the head of the astragalus—open reduction, Frank S. Child (by invitation).

II. PAPER OF THE EVENING—Some physiological considerations concerning fracture healing, Robert W. Johnson, Baltimore (by invitation).

III. DISCUSSION—Fred H. Albee, Clay Ray Murray, John J. Moorhead.

SECTION OF OPHTHALMOLOGY—February 19

I. INSTRUCTION HOUR, 7 to 8 o'clock—Ophthalmoscopy, Arthur J. Bedell.

II. Demonstration Hour, 7:30 to 8:30 o'clock—a. Slit lamp studies, Milton L. Berliner, Isadore Goldstein, Wendell L. Hughes, Girolamo Bonaccolto (by invitation); b. Many cases with ocular fundus lesions; c. Binocular and hand ophthalmoscopes, Mr. Fairbain, Colonial Optical Co. (by invitation).

III. Section Meeting, 8:30 to 10:30 o'clock—a. Reading of the minutes; b. Case reports: 1. A case of choroidal atrophy without night blindness, Isaac Hartshorne—2. A case of Coate's disease, Richard T. Paton (by invitation)—3. Pathology of these retinal lesions, Bernard Samuels, projection by Edgar Burchell, M. Sc. (by invitation); c. Scientific paper: 1. Hereditary and familial degeneration of the macula, Ralph I. Lloyd; Discussors: 1. Henry H. Tyson, 2. Conrad Berens.

SECTION OF GENITO-URINARY SURGERY—February 21

I. Scientific Program from the Urological Department of the Morrisania City Hospital—a. Urological staff organization at Morrisania City Hospital, C. Travers Stepita; b. Perforation of ureter by a calculus. A case report, Succorso A. Suriano (by invitation); c. Gangrenous cystitis eventuating in cystotomy. A case report, Maximillian Zigler (by invitation); d. Silent renal and ureteral calculi. With lantern slide demonstration, Joseph Schwartz; e. Recto-urethral fistula with involvement of seminal vesicle. Demonstration of patient, John W. Rogers (by invitation); f. Traumatic rupture of solitary kidney. A case report, John Roth (by invitation); g. Electrosurgery in urology, Daniel A. Sinclair (by invitation); h. Unusual tumor of adrenal with destruction of kidney. A case report, J. J. Valentine: Discussion to be opened by William Aronson (by invitation); i. Branching calculus and hypernephroma of kidney. A case report, Angel F. Golderos (by invitation); j. Perinephritic inflammations and suppurations, John Duff; k. A review of prostatic surgery at Morrisania City Hospital, 1930-1933, John Toole.

COMBINED MEETING OF THE SECTION OF OTOLARYNGOLOGY *and the* SECTION OF PEDIATRICS—February 21

I. Case Presentation—Two cases of pharyngeal hematoma and hemorrhage, William Spielberg.

II. Papers of the Evening—a. Hematoma and hemorrhage of the pharynx and peritonsillar area, Samual Salinger, Chicago (by invitation); b. Progress in tonsil surgery, illustrated by slides and motion pictures, a resume of 25,000 cases, Robert H. Fowler; c. Personal observations on the after-effects of tonsillectomy, Murray H. Bass, Howard H. Mason; d. Practical considerations of diseases of the nasal accessory sinuses in children, William Mithoefer, Cincinnati (by invitation); Discussion opened by Herman Schwarz, Charles J. Imperatori.

III. General Discussion. IV. Executive Session.

SECTION OF OBSTETRICS AND GYNECOLOGY—February 27

Program arranged by the Obstetrical Staff of the Fifth Avenue Hospital

I. Presentation of Cases—Preventative pre-natal treatment of melena neonatorum in successive pregnancies, John E. Tritsch (by invitation); Discussion to be opened by I. Newton Kugelmass (by invitation).

II. Papers of the Evening—a. Dysmenorrhea in industry, Frances E. Shields (by invitation); Discussion to be opened by Emily D. Barringer; b. Some urethral conditions in women (lantern slides), H. Dawson Furniss; Discussion to be opened by Sophie Kleegman, E. Barringer; c. Present status of obstetric anesthesia, analgesia and amnesia, Leon S. Loizeaux; Discussion to be opened by T. Drysdale Buchanan (by invitation), Paul N. Wood.

III. General Discussion. IV. Executive Session.

AFFILIATED SOCIETIES

NEW YORK ROENTGEN SOCIETY *in affiliation with* THE NEW YORK ACADEMY OF MEDICINE—February 19

I. 8:00 to 8:30 p. m.—Demonstration and discussion of interesting cases.

II. 8:30 p. m.—Symposium on indications for roentgentherapy in malignant disease of the ear, nose and throat; Presentation of cases, Maurice Lenz (previously shown to this society) (30 minutes); Microscopic structure, A. P. Stout; Cancer of the nose, A. A.

Schwartz; Cancer of the ear, J. D. Kernan; Cancer of the larynx, R. E. Buckley; Cancer of the oropharynx, including cervical gland metastasis, G. H. Semken (10 minutes each); Discussion to be opened by Francis C. Wood, Hayes E. Martin, A. L. L. Bell. All cases will be available for examination at 8:00 o'clock.

III. GENERAL DISCUSSION. IV. EXECUTIVE SESSION.

NEW YORK MEETING OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE *under the auspices of* THE NEW YORK ACADEMY OF MEDICINE—February 21

I. Changes in the hypopthysis of adult male and female rats after prolan injection, A. E. Severinghaus.
II. Reduction of methylene blue by the blood of young infants, Carl H. Smith.
III. Therapeutic type VIII (Cooper) serum: its efficiency and reactions, J. G. M. Bullowa.
IV. A type-specific substance from the meningococcus, H. W. Scherp, G. Rake.
V. Chemical studies in bacterial agglutination. I. A micro method for the quantitative estimation of agglutinins, M. Heidelberger, E. A. Kabat.
VI. Bacterial variation in pneumococcus and streptococcus hemolyticus, M. H. Dawson; Introduced by A. R. Dochez.
VII. Anaphylactogenic properties of purified milk proteins, raw, evaporated, superheated, dried and acidified milk, B. Ratner, H. L. Gruehl.
VIII. Metallic glutamates in nutritional anemia, E. Brand, C. J. Stucky.
IX. Specificity of enhancing material from mammalian tumors, A. E. Casey.

NEW YORK PATHOLOGICAL SOCIETY *in affiliation with* THE NEW YORK ACADEMY OF MEDICINE—February 22

I. DEMONSTRATION OF PATHOLOGICAL SPECIMENS.
II. PAPERS OF THE EVENING—a. Allergic inflammation of the lungs, B. M. Fried (by invitation); b. Dilatation of the pulmonary artery, (a) Idiopathic, (b) Associated with congenital cardiac anomalies, B. S. Oppenheimer; c. Dermatomyositis: a report of two cases, Sigmund Wilens (by invitation), Abner Wolf (by invitation); d. Giant cell leukemia, Paul Klemperer.
III. EXECUTIVE SESSION.

LIBRARY NOTES

RECENT ACCESSIONS TO THE LIBRARY

Beckman, H. Treatment in general practice. 2 ed.
Phil., Saunders, 1934, 889 p.

Dandy, W. E. Benign tumors in the third ventricle of the brain.
Springfield, Ill., Thomas, [1933], 171 p.

Falk, H. C. Operating room procedure for nurses and internes. [2. ed.].
N. Y., Putnam, 1934, 413 p.

Fishberg, A. M. Hypertension and nephritis. 3. ed.
Phil., Lea, 1934, 668 p.

Frazer, (Sir) J. G. The fear of the dead in primitive religion.
London, Macmillan, 1933, 204 p.

Globus, J. H. Neuroanatomy. 6. ed.
Balt., Wood, 1934, 240 p.

Grinker, R. R. Neurology.
Springfield, Ill., Thomas, [1934], 979 p.

Halliburton, W. D. & McDowall, R. J. S. Handbook of physiology. 33. ed.
Phil., Blakiston, [1934], 971 p.

Nicholson, D. Laboratory medicine. 2. ed.
Phil., Lea, 1934, 566 p.

Ray, M. B. Rheumatism in general practice.
London, Lewis, 1934, 404 p
Rose, (Mrs.) M.D. (Swartz). The foundations of nutrition. Revised ed.
N. Y., Macmillan, 1933, 630 p.
Seldin, H. M. Practical anesthesia for dental and oral surgery.
Phil., Lea, 1934, 525 p.
Stannus, H. S. A sixth venereal disease
London, Baillière, 1933, 270 p.
Tuffier, T. Titres et travaux scientifiques
Paris, Jouve, 1933, 290 p.
Whitnall, S. E. The study of anatomy. 2 ed.
London, Arnold, 1933, 93 p.

Books by Fellows

More than ever, we need gifts of books for the Library, as our funds are much decreased. The Library Committee would be very pleased if all Fellows would present copies of their newly published works to the Academy. Many have been kind in this way in the past, and the Library Committee offers them its sincere thanks.

FELLOWS AND MEMBERS ELECTED FEBRUARY 1, 1934

FELLOWS

Roland I. Grausman	130 West 58 Street
Louis Charles Rosenberg	11 Murray Street, Newark, N. J.

MEMBERS

Myron A. Sallick	1125 Park Avenue
Louis H. Barenberg	1749 Grand Concourse
Arthur S. Calman	1160 Park Avenue
Coleman B. Rabin	1233 Park Avenue
John Alfred O'Regan	983 Park Avenue
Janet Travell	9 West 16 Street

Dennis, Frederic Shepard, M.D., 1136 Fifth Avenue, New York City; graduated in medicine from Bellevue Hospital Medical College in 1874; elected a Fellow of the Academy May 1, 1879; died March 8, 1934. Dr. Dennis was a Fellow of the American Medical Association and a member of the County and State Medical Societies. He was a Fellow of the Royal College of Surgeons and the American College of Surgeons; a member of the Clinical Society of London, the German Congress of Surgeons and a member and former president of the American Surgical Association. For twelve years he was Professor of Clinical Surgery at Cornell Medical College and held the same chair at Bellevue Hospital Medical College from 1883 to 1898. Dr. Dennis was one of the first surgeons in the United States to demonstrate the Lister Theory of Antisepsis. He was one of the founders of Harlem Hospital and at the time of his death was Consulting Surgeon to Bellevue, St. Vincent's, Montefiore and Litchfield County hospitals.

Lambert, Frederick Ellsworth, M.D., 157 Ocean Avenue, Jersey City, New Jersey; graduated in medicine from the Long Island Hospital Medical College, Brooklyn, New York, in 1894; elected a Fellow of the Academy April 4, 1907; died, March 1, 1934. Dr. Lambert was a Fellow of the American Medical Association and a member of the County and State Medical Societies. He was Attending Physician to Christ Hospital in Jersey City.

Spaulding, Edith Rogers, M.D., 103 East 86 Street, New York City; graduated in medicine from Tufts College Medical School, Boston, in 1909; elected a Fellow of the Academy February 3, 1921; died February 23, 1934. Dr. Spaulding was a Fellow of the American Medical Association, a member of the County and State Medical Societies, the American Psychiatric Association, the American Psychopathological Association, the Neurological Society, the New York Society for Clinical Psychiatry and the Psychoanalytical Society of New York. She was Assistant Psychiatrist to Vanderbilt Clinic.

BULLETIN OF
THE NEW YORK
ACADEMY OF MEDICINE

VOL. X APRIL, 1934 No. 4

ANNUAL REPORT FOR THE YEAR 1933[1]

PRESIDENTIAL ADDRESS[2]

Activities of the Past Year

Members and Fellows of the Academy:

It is my good fortune to be able to assure you that the Academy of Medicine has come through this troublesome year of 1933 with flying colors, maintaining its proud position as a leader in the promotion of medical science in this country, and a staunch defender of the health and welfare of this community. It stands in the forefront of the battle to promote the economic status of the physician in this era of change and of depression from which we are fortunately emerging; more than that, it upholds the highest standards of medical ethics.

It will not countenance any infringement of the code by which the medical profession has maintained its dignity, and, as President, I am happy to say that the Committee on Admissions, the Committee on Professional Standards, the Committee on Fellowship, are set firmly against any candidate, member or fellow, known to resort to questionable methods in practice.

Fee splitting *must* disappear from the medical ranks. The Committee on Professional Standards has made its

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[1]The following reports were presented at the Annual Meeting of the Academy, January 4, 1934.

[2]This address comprises the Annual Report of the Council for the year 1933.

position clear, and I would advise any who are in doubt as to what the Academy would do in a given case, to read the resolutions of the Committee on Professional Standards, as published in the Bulletin for February, 1933, on page 331.

In my Inaugural Address a year ago, I hoped for the restoration of the influence of the family practitioner, and for the more careful designation of the specialist for the special purpose of protecting the public. A Fellow in a Section of the Academy of Medicine endorsed by the members in that Section, was thought to be qualified as a specialist in that very field, if recommended by the Committee on Fellowship and approved by the Council.

Progress had been made along that line, when to the Council's surprise, some opposition was offered. The Academy is progressive, eager for reform when reform is needed, but not stubborn. It is therefore still studying, or, again studying, this question of Fellowship. A special sub-committee has been appointed and after the Council has received and discussed that sub-committee's report, the whole matter will be presented to the entire membership.

The main question is, has the Academy directly or by implication, the right to put upon any one of its members, or to withhold from such member, the stamp of specialist. The question is still sub judice. Our action on that matter will have an important bearing upon the relation of the Academy to the public.

In the truest sense of the word, we are honestly and sincerely hoping to protect the health and safety of the community.

It has been known for years to the Public Health Relations Committee, and to the obstetrical organizations of this City, that the maternal mortality statistics of this City were unfavorable. It was the duty of the profession to remedy, if possible, any evils for which the medical and

obstetrical practitioner might be responsible. A thorough study was undertaken with the cooperation of some of the foremost obstetricians of the City, and with the support of the Commonwealth Fund.

A carefully drawn report was submitted, revealing a discouraging state of affairs. Protest has been entered against the mode of publicity. This needs neither defense nor further comment from me. All the members have received a satisfactory explanation in the report of the sub-committee consisting of Drs. John A. Hartwell and Samuel W. Lambert, and approved by Dr. Sondern, Chairman of the Sub-Committee on Maternal Mortality, and the Obstetrical Advisory Committee; the Council has also given its unanimous approval to this Sub-Committee's report, and that report has been mailed to the entire membership of the Academy. Let me hope that all of you have read it carefully.

The publicity protest is of minor significance as compared with the startling nature of the facts disclosed in the Report itself. The Academy hopes that these facts will be carefully discussed at a special meeting soon to be arranged for the sole purpose of bringing about an improvement in obstetrical practice. Our methods of publicity are not wholly satisfactory. A sub-committee has been appointed to report on *that* subject, and I have no doubt that its recommendations will seek to remedy any existing evil.

In this Academy, the two hundred or more men, assiduously working for its good, are just human. They may err at times, and if so, they are rabid for reform. The Council and the Committees speak for the entire membership of the Academy. They do not speak for the entire medical profession, but they have reason to believe that the greater part of the lay and medical public in this community have faith in the opinions of the Academy. Those opinions will be uttered fearlessly in the future, as in the past, with sole reference to the welfare of the entire com-

munity. The Academy will, however, refuse to take part in any political strife.

During the last few months, the work of the Academy has been made more difficult in consequence of the protracted illness of its able director, Dr. Linsly R. Williams. All of us have been made to realize the importance of his office, and the unique way in which he had developed it. Dr. Hartwell has accepted the Council's invitation to act as Interim Director.

The main purpose of the Academy is to further the advancement of medical science. In that respect, the work done by the various Sections of the Academy, and the closer cooperation between the Sections have been most gratifying. During the past year, notable work has been done in the thorough study of diabetes in all its phases. But, most satisfactory of all, was the elaborate program offered and the many discourses presented during the Graduate Fortnight on Disorders of Metabolism, not to omit mention of an exhibit which did great credit to those who participated in the arrangement of the Fortnight. It will be the aim of the Committee on Education to maintain the high standards set in 1933, and the announcements for the 1934 Fortnight will soon be forthcoming.

In view of the length of our evening's program, I have only singled out a few topics for immediate comment. The reports of the various committees will describe the detailed work of this beehive of medical endeavor.

I must make brief reference to the excellent Report of the Committee on Workmen's Compensation to His Excellency, the Governor, in which Dr. Pool and his associates have done splendid work.

During the past year, death has taken more than a fair toll of our membership. A number of them have left us in what appeared to be the prime of life, and in the midst of their useful activities. Among those we have lost have been several officers of the Academy, and men and women of deserved prominence. Out of respect to the

memory of these men, who have been taken from us, I would ask this audience to rise and stand for a brief silent moment.

BERNARD SACHS, *President.*

REPORT OF THE BOARD OF TRUSTEES

In December, 1932, the Trustees adopted the budget for the year 1933 of $236,296.44 and estimated that for the year 1933 the total income available for the general activities of the Academy would amount to $238,650.00. The estimated income proved to be in excess of the actual income by $6,619.26 which was brought about by the very unsatisfactory condition of negotiable securities and the bond and mortgage situation. However, by very close supervision on the part of the administration it was possible to operate within this income by cutting the total expenditures to $230,468.02 and thus leave a small balance at the end of the year. This was accomplished despite the fact that on several occasions during the year a checking of expenditures against receipts indicated that there might be a deficit of approximately $4,000. The satisfactory result of the year's operation was accomplished by the very hearty cooperation of all departments in keeping expenses to the lowest point compatible with efficient operation. The Trustees desire here to formally express their appreciation of the spirit with which the entire staff cooperated in this work of economy and the cheerfulness with which they accepted their pro rata decrease in salaries. Details will be found in the Report of the Treasurer.

The Trustees take very great pleasure in reporting the opening of the new extension on October 11th, since which time it has been in full operation. The activities carried on within it fully demonstrate the wisdom and foresight on the part of Dr. Williams in having urged its undertaking. The Report of the Building Committee herewith appended presents a detailed account of the additional

facilities and the uses they may be put to. The operation of this additional space has been conducted without any addition to the staff and very slight addition to overhead charges, an accomplishment which again illustrates the spirit of cooperation which characterizes the conduct of the Academy.

The Trustees beg to report that at the close of the year the depreciation in values of our capital holdings and the income therefrom seems to have become stabilized and that steps are being taken under the best financial advice procurable to overcome the fiscal difficulties which face the Academy as well as all similar institutions.

EUGENE H. POOL, *Chairman.*

BUDGET 1934

Income Estimated

Investments	$115,000.00
Dues—Members	69,500.00
" —Library	1,100.00
Contributions	12,700.00
Room Assessments	14,500.00
Bibliography and Photostat	4,600.00
Estate—Witthaus	5,800.00
Graduate Fortnight	2,700.00
Academy Bulletin	3,900.00
Surgical Bulletin	900.00
Bank Interest	300.00
Health Examiner	8,100.00
Total	$239,100.00

Expenses Estimated

Administration—Salaries	$ 26,600.00
" —Expenses	4,950.00
Corporation Expense	12,490.00
Building Operation—Salaries	28,615.10
" " —Expenses	14,950.00
Library—Salaries	55,297.10
" —Expenses	24,500.00
Medical Education—Salaries	12,427.80
" " —Expenses	12,150.00

Sections—Salaries	5,705 00
" —Expenses	10,715.00
Public Health—Salaries	14,029 00
" " —Expenses	700.00
Press Relations—Salaries	6,674 80
" " —Expenses	8,700 20
Total .	$238,504.00

The following gifts and bequests have been received during the year:

Gifts and Bequests

Endowment

Purpose	*Donor*	*Amount*
Rare Book Fund	Linsly R. Williams	$ 30.00
General Library Endowment	Carnegie Corporation	26,250.00
Library Endowment	Mrs. Stafford McLean	10,000 00
" "	Estate of Frederic Kammerer	10,000.00
Bacteriology and Sanitary Science	Louis Livingston Seaman Estate	2,603 13
Total New Endowment		$48,883 13

Current Expenses and Special Funds

General Library Expense	Anonymous	$10,000.00
New Books	Mrs. Walter Brickner	150.00
" "	Mr. and Mrs. Henry Wittkowski	10.00
Foreign Scholarships	Mrs. Alex. Cochran Bowen	4,000.00
British Museum Catalog	Samuel W. Lambert	200.00
Books on Dentistry	First District Dental Society	500.00
Library Publication Fund	Marcia Brady Tucker	5,000.00
" " "	L. K. Thorne	1,000.00
" " "	Robert Sterling Clark	2,150 00
" " "	Wm. B. Osgood Field	100 00
Medical Information Bureau	Milbank Fund	2,500.00
Sections	Douglas Quick	100.00
"	Anonymous .	100.00
Total Contributions Current Expenses		$25,810.00
Total Gifts		$74,693.13

The following have been received during the year:

BUILDING FUND YEAR 1933

Received from Fellows:

1 at $4,150	$4,150.00	
1 at 1,500	1,500.00	
1 at 750	750.00	
1 at 525	525.00	
1 at 500	500.00	
1 at 250	250.00	
3 at 200	600.00	
3 at 100	300.00	
2 at 50	100.00	
7 at 25	175.00	
1 at 15	15.00	
2 at 10	20.00	
Total from Fellows		$8,885.00

From Non-Fellows:

E. S. Harkness	$210,000.00
Marcia Brady Tucker	1,000.00
Comprex Oscillator Co. (Joseph F. McCarthy)	300.00
Mrs. A. Wineburgh (Edwin Beer)	100.00
Joseph Lilienthal (Edwin Beer)	100.00
Edwin H. Stern (Marcus A. Rothschild)	100.00
Sidney Borg (Edwin Beer)	100.00
Mrs. Sophie Beer (Edwin Beer)	100.00
Edgar A. Levy (Marcus A. Rothschild)	100.00
Clarence F. Mackey (Foster Kennedy)	50.00
Frederick Warburgh (Edwin Beer)	50.00
Lucy Stedman (Foster Kennedy)	25.00
Mrs. Alice Carns (Edwin Beer)	25.00
Total received year 1933	$220,935.00

ALLOCATION OF FELLOWS' DUES FOR 1934

1. Building Operation—Salaries	$ 28,615.10
" " —Expenses	14,350.00
2. Sections and Stated Meetings—Salaries	5,705.00
" " " " —Expenses	5,000.00
3. Membership Bureau; Comptroller; Subscriptions to Bulletin	4,000.00
4. Library	11,829.90
Total sum to be received	$ 69,500.00

EUGENE H. POOL, *Chairman.*

ABSTRACT OF TREASURER'S REPORT

I have the honor to present The New York Academy of Medicine Statement of Assets and Liabilities as at December 31, 1933, as follows:

ASSETS

Cash in Bank and on hand		$ 51,005.96
Investments:		
Mortgages	$1,228,325.00	
*Stocks (Market $500,671.25)	918,999.25	
*Bonds (Market $491,576.25)	733,968.76	
Real Estate	135,258.20	3,016,551.21
Due From:		
Lawyers Mortgage Company		1,226.92
Bank of New York and Trust Company		949.15
R. A. Witthaus Estate		3,585.01
Charles A. Powers Estate		1,513.98
Fixed Assets:		
Academy Land and Building	$2,228,292.95	
Library	678,476.31	
Equipment and Portraits	191,999.49	3,098,768.75
Deferred Assets and Prepaid Expenses:		
Unexpired Insurance Premiums	$ 1,303.50	
Committee on Nomenclature of Diseases	502.32	
Prepaid Advertising Commission	422.94	
Maternal Mortality Committee	52.55	2,281.31
Total Assets		$6,175,882.29

LIABILITIES

General Property Fund	$2,716,948.22
Endowment Fund	1,311,510.47
Educational Endowment Fund	1,250,000.00
Building Fund for New Addition	369,086.07
Library Funds	235,411.17
Thomas W. Salmon Memorial Fund	100,000.00
Edward N. Gibbs Memorial Prize Fund	21,482.57
Public Health Relations Reserve Fund	18,268.21
Academy Rare Book Fund	12,146.10

*List may be reviewed by members upon application to the Director or the Treasurer's office.

Alfred Lee Loomis Entertainment Fund	11,000.00
William S. Halsted Fund	10,000.00
Louis Livingston Seaman Fund	7,007.22
Wesley M. Carpenter Fund	5,813.09
Hermann M. Biggs Lectureship Fund	4,000.00
Academy Medal Fund	3,000.00
L. Duncan Bulkley Lectureship Fund	2,000.00
Ernst Hermann Arnold Fund	543.98
Reserve Fund	73,910.50
	$6,152,127.60
Accounts Payable (1933)	8,354.36
Employees Annuity Reserve	2,100.01
Deferred Income (1934 Dues)	132 50
Trust Funds	13,167.82
Total Liabilities	$6,175,882 29

Statement of Income and Expense

INCOME

Investments		$ 103,719.76
Dues Members	69,683.56	
Library	1,130.00	70,813.56
Room Assessments		14,272.29
Anonymous 1933 Expense Contribution		10,000.00
Bulletins		7,329.62
Bibliography and Photostat		4,242 80
Bank Interest		845.22
Administration Fees—Bowen, Salmon and Health Examiner Funds		607.18
Messenger Fees and Miscellaneous		95.40
		$211,925.83
Restricted:		
Library Funds	$12,419.81	
Graduate Fortnight	2,618.71	
Contributions for Book Purchases	160.00	
Reserves Consumed	4,425.99	19,624.51
		$ 231,550.34

EXPENSE

Administration and General	$42,159 64	
Building Operation	47,561.23	
Library	79,424.75	
Medical Education	29,143.38	
Public Health	14,676 62	
Sections	10,583 44	
Press Relations Bureau	7,285.99	230,835 05
Transferred to Special Reserve Fund		715.29

Statement of Special Funds

Balances December 31, 1933

For the General Purposes of the Library

The Library Fund—Balance January 1, 1933 (including bequests of Joseph D. Bryant, $5,618 18; E. B. Bronson, $5,000.00; and Carnegie Corporation, $8,750.00)	$ 56,870.07
Add: Gift from Carnegie Corporation	26,250 00
Bequest, Estate of Frederic Kammerer	10,000.00
Gift from Mrs Stafford McLean	10,000 00
Sale of Triplicates	35 10
	$103,155 17

Landon Carter Gray Memorial Fund. Established 1911	$ 50,000 00
Anna Woerishoffer Fund Established 1897	15,000.00
Horace Putnam Farnham Fund. Established 1889	10,000 00
German Hospital and Dispensary Fund. Established 1903	3,000.00
James S. Cushman Fund. Established 1897	1,000 00
Orville Ranney Flower Fund. Established 1897	1,000 00
William T. Lusk Memorial Fund. Established 1893	1,000.00
Albert William Warden Fund. Established 1906	1,000.00
J. Marion Sims Memorial Fund. Established 1896	100.00
Rudolph A Witthaus Fund. Legacy of Rudolph A. Witthaus, M.D Established 1917. Principal not received by Trustees; will approximate $190,000.	

Library Funds Restricted to Book Purchases

Everett Herrick Fund. Established 1915	$ 25,000.00
Philippine Meyer and Ernst Jacobi Fund. Established 1915	14,486.00
Ernst Krackowizer Fund. Established 1897	2,000 00
Austin Flint Memorial Fund. Established 1910	1,200.00
Merrill Whitney Williams Fund. Established 1895	220.00

Library Funds Restricted to Purchases of Special Books

L. Duncan Bulkley Fund. Income to be used for the purchase of books on Cancer. Received 1929		$ 5,000.00
F. Bullowa Memorial Fund. Income to be used for the purchase of books relating to the Ductless Glands. Established 1919.		1,000.00
James P. Tuttle Fund. Income to be used for the purchase of books on Diseases of the Digestive Tract. Established 1913.		1,000.00
A. L. Northrup Dental Fund. Gift of the First District Dental Society, N. Y. Income to be used for the purchase, binding and care of books on Dentistry. Established 1897		250.00
Academy Rare Book Fund Balance, January 1, 1933	$12,112.60	
Add: Sale of Cardozo Books	3.50	
Gift from Linsly R. Williams	30.00	12,146.10
		$ 247,557.27

Funds Restricted to Special Uses

Thomas W. Salmon Memorial Fund from Thomas W. Salmon, Inc., to establish fund		$ 100,000.00
Wesley M. Carpenter Lectureship Fund. Income to be used annually for one medical lecture. Established 1891		5,813.09
Hermann Michael Biggs Lectureship Fund, Received from Mrs. Biggs and New York Tuberculosis and Health Association in 1930. Income to be used for lectures on Public Health and Preventive Medicine		4,000.00
L. Duncan Bulkley Lectureship Fund. Income to be used for lectures on Medical Aspects and Treatment of Cancer. Established 1929		2,000.00
Educational Endowment (Rockefeller Foundation)		1,250,000.00
Academy Medal Fund (Dr. Samuel McCullagh)		3,000.00
Building Fund for New Addition:		
Balance January 1, 1933	$148,151.07	
Add: Receipts 1933	220,935.00	369,086.07
Edward N. Gibbs Memorial Prize Fund. Income to be awarded to a research worker on Diseases of the Kidney. Established 1901.		21,482.57
Public Health Relations Reserve Fund		18,268.21
Alfred Lee Loomis Entertainment Fund.. Established 1895		11,000.00
Louis Livingston Seaman Fund for Bacteriology and Sanitary Science:		
Balance January 1, 1933	$4,404.09	
Received in 1933	2,603.13	7,007.22
Ernst Hermann Arnold Fund. Income to be used for Section on Orthopedics. Established 1932.		543.98

Unrestricted General Funds

General Property Fund. Balance January 1, 1933 (including bequest of Celine B. Hosack, \$70,000.)		\$2,695,275.03	
Add: Library Additions for 1933		21,189.86	
Equipment		483.33	2,716,948.22
William S. Halsted Fund. Established 1930.			10,000.00
Endowment Fund, Balance January 1, 1933		\$1,364,190.25	
Including gifts and legacies of:			
Everett H. Herrick	\$25,000.00		
Walter B. James	25,000.00		
Libbie V. Wagner	25,000.00		
Mrs. Harry Payne Whitney	25,000.00		
Milbank Memorial Fund	10,000.00		
W. Gilman Thompson	10,000.00		
Raymond Guiteras	4,911.80		
Seth M. Milliken	3,000.00		
John T. Nagle	2,500.00		
William K. Vanderbilt	2,500.00		
Louis F. Bishop	320.00		
Add: Admission Fees		4,545.00	
Sale of Equipment		10.00	
		\$1,368,745.25	
Loss through Sale of Securities		57,234.78	1,311,510.47
Reserve Fund, January 1, 1933		\$ 74,851.78	
Deduct: Transfer from Graduate Fortnight to Nomenclature Committee		2,500.00	
		\$ 72,351.78	
Add: Certificate Fund, Reserved		275.00	
Health Examiner Surplus		568.43	
1933 Reserve Fund Addition		715.29	73,910.50
			\$6,152,127.60

Seth Milliken,
Treasurer.

AUDITOR'S CERTIFICATE

(Page 9 of their Report)

We have audited the books and accounts of The New York Academy of Medicine for the year ended December 31, 1933, and hereby certify that the Balance Sheet and Statement of Income and Expense herewith submitted, in our opinion, correctly reflect the financial condition as at December 31, 1933, and the results of operations for the year under review, the accounts being kept on a cash basis.

Respectfully submitted,

MILLER, DONALDSON AND COMPANY.

THE ADDITION TO THE ACADEMY OF MEDICINE

REPORT OF THE BUILDING COMMITTEE AS PREPARED BY MR. LOUIS AYRES OF YORK & SAWYER, ARCHITECTS

Early in 1929 it was becoming evident that the growth of the Library as well as other parts of the Academy would before long require additional space.

The original building was constructed so that future stories could be superimposed and additional property had also been acquired to the east of the low rear wing which housed Hosack Hall two stories high and the work rooms of the Library on the third floor level. The only obvious way to increase the Library with fairly adjacent space without disrupting the second floor was above and possibly beyond the rear wing.

The first tentative drawings, the principal feature of which was a Rare Book Room, were started by the architects in July of 1929 and in August a perspective of the interior was made to stimulate the interest of the members.

In December of 1930 The Council authorized a more thorough study resulting in several schemes being submitted to the Building Committee in March, 1931. One which included the then vacant 25 foot lot in the rear was most liked as it gave needed additional space on the Library floor, a better scheme for the Rare Book Room on the mezzanine level above the Library, and made it possible to prepare for the enlargement of Hosack Hall if necessary in the future. This scheme and a smaller one were then further studied and preliminary estimates obtained which were submitted in May, $450,000 for the larger and $350,000 for the smaller. The Building Committee recommended to the Council the larger scheme.

Due to difficulties in raising the difference between the estimates for this scheme and the amount of $350,000 promised by Mr. Harkness, the architects worked with Dr. Williams throughout the Summer of 1931 to keep the main features of the larger scheme and reduce the cost. This was done and the budget fixed at $400,000 on November 10th, and on November 25, 1931 the architects were authorized to proceed with final working drawings and specifications and Marc Eidlitz & Son, Inc., to proceed with the construction of the building.

The addition though not very large in volume was a rather difficult problem in construction and working conditions. In part built on top of the existing and inhabited library work rooms, the balance included foundation and structure on the 25 foot lot to the east. As was discovered when the original building was constructed, the underlying rock sloped from the street level at Fifth Avenue rapidly downward to the rear. The conditions in the 25 feet referred to were found to be much worse than in the rear portion of the original building, solid rock was 50 feet below street level and this had apparently been used as a dump for all kinds of boulders, old ironwork, etc. The apartments to the east owned by the Academy were pretty shaky and their foundations had to be underpinned, an extremely difficult matter under aforesaid conditions

and with the extremely narrow space between the two buildings. Another difficult matter of construction was the changing of construction of the original east wall of the extension, taking out the steel columns and substituting another truss similar to those over Hosack Hall to allow for its future extension into the space now to be used for exhibition rooms on the first and second floor.

These complications not seeming sufficient to an "All Wise Providence" a month or two of strikes delayed the starting of steel erection till October 3, 1932. Rapid progress was made from then on which included also various changes in the original building and the work was practically completed in the spring of this year (1933).

The Academy has gained the following much-needed accommodations by this extension:—Three exhibition rooms, basement, first and second floors east of Hosack Hall, each approximately 24′0″ x 54′0″ (these rooms are inexpensively finished with colored cement floors, walls sheathed with plank and hung with loose woven "monks cloth" and the ceilings plastered directly on the constructional work); additional work rooms on the Library (third) floor to the east; the Rare Book and Reference Room; Librarian's Suite; Portrait; Drafting; 6 Study Rooms (in addition to 5 old study rooms); various toilets, fan rooms, etc., on the third mezzanine together with a special stair connecting this floor with the Library (third) floor.

On the fourth floor are the offices of the Committee on Public Health Relations, the First District Dental Society, and four other offices; 13 rooms in all. The fifth floor contains the new suite for the Council, a kitchen, dining room, four office rooms and a committee room. The suite for the Council consists of a small lobby with coat closet and telephone booth and adjoining it a committee room and the Council Room. The Council Room is 22′0″ x 35′0″ paneled in butternut to the ceiling (which is of acoustical plaster). Warm colored carpets and draperies are used and the furniture

from the old Council Room with a few additions. It seats 18 at the long T-shaped table and 22 more around the sides of the room. The Committee Room (13'0" x 18'0") seats 10 at the table and is similarly furnished except that it is not paneled but papered and painted in harmony with the Council Room.

The Dining Room on the south side can seat and serve at one sitting about 36. The dining room, opening directly from the kitchen, has walls of the same green as the kitchen fixtures and yellow curtains. The kitchen which is designed to take care of a hundred persons in the future is tiled to the ceiling in yellow and the iceboxes, cabinets, etc., done in green. The alternate squares of black and buff linoleum run through both rooms.

The principal feature of the extension and the most difficult in planning, is the new Rare Book and History Room with its various related offices. Much study was given to this problem, by the Building Committee, Dr. Williams, Dr. Malloch and the architects, and the result seems satisfactory to everyone.

The only available space which could be used and made convenient of access by the new stair to the Library proper was the third mezzanine floor which, in the original building, was small and with low ceilings. It was occupied by small study rooms, fan rooms, etc.

By remodeling the elevator hall and corridor, raising the story height in the extension, and by making the very long and narrow corridor attractive by decoration and framed prints, the approach to these rooms has been made most attractive.

The main room itself, the Rare Book and History Room, is 22 x 50 feet from wall to wall and divided on the north side into three wide and shallow alcoves formed by book shelves at each of the three big windows.

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The entire room is shelved to the ceiling with selected English oak of a fine color and marking, with narrow carved pilaster and carved frieze which is pierced in certain portions forming ventilation registers. The rare books are protected by bronze grille doors of a small mesh and light appearing construction, not interfering with the visibility of the books. The purpose of the department is not merely to provide a treasure room for the valuable books but to house also any reference works in biography, bibliography or medical history that might be of assistance to anyone working with the source of material in the early volumes. These "tools" are kept upon open shelves. The latter have been so constructed that in the future grille doors may be added if more space is needed for the rare books.

The lighting of the faces of the shelves from floor to ceiling was a serious problem and after much experimentation chandeliers were designed which have both direct light downward and reflectors which throw light on the ceiling from where it is reflected in turn to the books which form the walls. These two different lightings are controlled by separate switches in each of the three fixtures so they can be used together or separately.

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...e furniture especially designed for the room is of ...t slightly darker than the oak of the room. There ...o large atlas cases of English oak, which stand under two of the chandeliers, the top forming a ... desk for using the large atlases they house. Two ... tables back up against these cases, two desks, ...f the members of the staff who are engaged in cataloguing, occupy one alcove and readers'

tables the other two. There is a circular table in the center of the room. Four small glass covered stands at the sides of the room are for exhibition of books. The room has a fine character, is workable and pleasant to be in.

Adjoining to the west is the Seminar Room, 15 x 22 feet, really a part of the main room and duplicating it in treatment but separated from it and furnished so that it can be used for this purpose.

The other end has two rooms, for Dr. Malloch, the Librarian, off the first of which is the small book vault for the most valuable books, a small book lift down to the Library work rooms and a small locker, supply and wash room for his assistants.

This floor has a 12 foot setback on the street front which tends to prevent street noises to be heard in the Rare Book Room, Seminar Room and Dr. Malloch's offices which face the street. This terraced setback is paved with red roofing tile and is accessible through doors and windows.

The main room and seminar together have a capacity of 1,450 running feet of shelving spaced 12 inches high. The shelves are adjustable and portions have a shelf omitted giving necessary height for folios.

Full air conditioning of these rooms was considered by all to be too expensive and unnecessary, the system installed providing for forced ventilation (a change of air four and a half times each hour) combined with direct radiation at each window, the forced air being humidified and tempered and all controlled by thermostats and humidostats.

On the other side of the corridor are small work rooms, a drafting room for artists working with atlases and anatomical drawings, and a room for separate portraits, prints, etc., toilets and fan rooms and, at a slightly higher level (served by the new stair from the library floor), are four new study rooms built on top of the stack. When expansion of the stacks is necessary, it will be easily pos-

sible to add extra floors. If the Rare Book department requires facilities of this kind, the adjacent stacks can be wired off for the protection of the books.

Various changes and refurnishings have also been accomplished in the original building and in the planning of the new floors, it has been kept in mind that the Academy owns the property to the east and that future extension might take place there.

The exterior of this extension is of stone matching the old building and harmonizes with its design.

ARTHUR B. DUEL, *Chairman, Building Committee.*

REPORT OF THE COMMITTEE ON ADMISSION

The Committee on Admission reports to the Academy that during the past year 131 applications for membership were considered. Of these 99 were recommended for Resident Fellowship, 12 for Resident Membership, 5 for Non-resident Fellowship, 2 for Associate Fellowship and 3 for Associates; 10 applicants were dropped.

The Committee met each month except during the summer and reports an attendance of nearly 100 per cent. On December 31, 1933, there were 24 vacancies. There are 5 applicants for Fellowship, 48 for Membership, and 1 for Associate now before the Committee.

The Committee seeks the cooperation of the Fellows in asking that they give support to candidates believed to be desirable, and write as fully as possible in regard to them. The Committee also asks that the Members and Fellows exercise greater care in considering whether or not they desire to support a candidate. It has happened on a number of occasions during the past that one or more of the sponsors of an applicant have withdrawn their approval of the candidate, either verbally or in writing, which is often embarrassing to the Committee.

HENRY ALSOP RILEY, *Chairman.*

REPORT OF THE COMMITTEE ON FELLOWSHIP

At the first Stated Meeting of 1933 the qualifications for Fellowship in the Sections as embodied in a revision of the Constitution and By-Laws of the Academy were voted upon and approved.

There was then formed the Committee on Fellowship consisting of twelve members, one in each of the various specialties as represented by the different Sections of the Academy, appointed by the Nominating Committee and elected by a vote of the Fellowship on March 2, 1933.

The first meeting of this new Committee was held on March 21st. This meeting and the two succeeding meetings were given over to the establishment of rules for the Committee to follow in the classifying of the present Fellowship and the application form to be used.

The Council approved of the Committee on Fellowship sending a special notice to the Fellows with the April folder, which announced that the Committee was organized, and in accordance with Section 6, Article XIII of the new By-Laws for 1933, was prepared to receive applications for the designation of Fellows in the various specialties as represented by the Sections.

The Committee on Fellowship reports to the Academy that from May to the end of 1933, 474 applications for special designation were received. Of these, 281 were recommended to the Council for approval; 242 of these Fellows were approved by the Council and received formal notice, the last 39 names included in the total number (which were the last to go to the Council for approval) were not considered owing to the action of the Council at its meeting of December 13th, that no more names would be considered until the whole plan was again brought before all the Section members for their advice and opinion of the present plan for classifying the Fellows of the Academy.

The Committee on Fellowship was delayed in passing upon many of the applicants owing to the death of Dr. Atkins, the resignation of Dr. Schloss and the unavoidable absence of one of the members who was able to attend only the first meeting of the Committee.

The Committee met on the third Tuesday of each month except June, July and August.

EDWARD L. KEYES, *Chairman.*

REPORT OF THE COMMITTEE ON LIBRARY

As we assumed that the depression accounted for some of the increase in readers during 1932 to the number of 47,042, so we blame partial recovery in 1933 for the decrease in readers to 45,031.

ADDITION TO THE LIBRARY

The important event of 1933 is of course the completion of the addition to the Academy building. This has given three exhibition rooms in what was the vacant lot on 103rd Street, more space for work-rooms for the Library staff on the main Library floor, and on the mezzanine floor a new Rare Book and History Room, a Seminar Room (which might well be called the "Little Room"), additional study rooms, drafting room for medical illustrators, and a Portrait Room to house the files of separate engravings and other portraits. All this was made possible by the magnificent gift of Mr. Edward S. Harkness, supplemented by subscriptions from Fellows and friends of the Academy. I cannot do better than quote from the account written by Mr. Louis Ayres of the firm of York and Sawyer, Architects, to whom Marc Eidlitz and Son, Inc., contractors, the work and design of construction was awarded. The result is very satisfactory to all concerned, for the beauty of the Academy building has been maintained and even enhanced by the addition. Mr. Ayres writes:

The Academy has gained the following much-needed accommodations by this extension: three exhibition rooms, basement, first and second floors east of Hosack Hall, each approximately 24'0" x 54'0" (these rooms are inexpensively finished with colored cement floors, walls sheathed with plank and hung with loose woven monk's cloth and the ceilings plastered directly on the constructional work); additional work rooms on the Library (third) floor to the east; the Rare Book and History Room; Librarian's Suite; Portrait; Drafting; 6 Study Rooms (in addition to 5 old study rooms); various toilets, fan rooms, etc. on the third mezzanine together with a special stair connecting this floor with the Library (third) floor.

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The main room itself, the Rare Book and History Room, is 22 x 50 feet from wall to wall and divided on the north side into three wide and shallow alcoves formed by book shelves at each of the three big windows.

The entire room is shelved to the ceiling with selected English oak of a fine color and marking, with narrow carved pilaster and carved frieze which is pierced in certain portions forming ventilation registers. The rare books are protected by bronze grille doors of a small mesh and light appearing construction, not interfering with the visibility of the books. The purpose of the department is not merely to provide a treasure room for the valuable books but to house also any reference works in biography, bibliography or medical history that might be of assistance to anyone working with the source of material in the early volumes. These "tools" are kept upon open shelves. The latter have been so constructed, that, in the future, grille doors may be added if more space is needed for the rare books.

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RARE·BOOK & HISTORY·ROOM·LIBRARY


NEW·YORK·ACADEMY·OF·MEDICINE

As the ceiling had to be nearly white and flat for reflecting purposes a modeled ceiling of very low relief was adopted similar to the English Elizabethan type and the design of the entire room more or less is based on this assumption. The floor for quiet and to avoid the necessity of rugs or carpets was made of cork in two shades and designed to resemble a parquetry floor.

The furniture especially designed for the room is of walnut slightly darker than the oak of the room. There are two large atlas cases of English oak, which stand directly under two of the chandeliers, the top forming a stand-up desk for using the large atlases they house. Two card-catalog tables back up against these cases; two desks, for the use of the members of the staff who are engaged in bibliographical cataloguing, occupy one alcove and readers' tables the other two. There is a circular table in the center of the room. Four small glass covered stands at the sides of the room are for exhibition of books. The room has a fine character, is workable and pleasant to be in.

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We learn from the architects that 6,721 square feet (98,243 cubic feet) have been added to the Library, which gives us a total of 22,916 square feet (386,248 cubic feet). These figures do not include 1,625 square feet (30,875 cubic feet) for the new exhibition room in the second floor extension, which is to house our historical museum containing old instruments, etc.

In charge of the Rare Book and History Department is Miss Gertrude L. Annan, who received her training in this field at the John Carter Brown Library, Providence, R. I., where she worked under Mr. Lawrence C. Wroth on the last part of the printed catalogue of that collection. A member of the Library staff was transferred to give full-time assistance in the Rare Book Department.

Gifts

This Committee acknowledges with gratitude the gift of $26,250 from the Carnegie Corporation towards endowment of the Library; $10,000 from Mrs. Stafford McLean in memory of her husband as a fund for the general purposes of the Library; $150 from Mrs. Walter M. Brickner for the purchase of new books in memory of her husband; and $10 from Mr. and Mrs. Henry Wittkowski for the purchase of a book in memory of the late Dr. Leroy Milton Yale.

The year that saw the Rare Book and History of Medicine Department installed in its new quarters was not without interest in the acquisition of books, manuscripts and memorabilia, through the generosity of friends and by carefully considered purchases. With the forthcoming atlas of Vesalian woodcuts in preparation, the work of the great anatomist is more than ever fresh in our minds. Through the kindness of Dr. Reginald Burbank we recently added another item of Vesaliana to our collection. *De Arthritidis Praeservatione et Curatione . . . Opera et Studio Henrici Garetii . . .*, Francofurti, apud Ioannem Wechelum et Petrum Fischerum, 1592, contains several of the "Concilia" of Vesalius. As very few of these "Concilia" have been pre-

served, either in whole or in part, we are more than delighted to have this volume. Dr. Alfred M. Hellman presented a copy of the rare first English edition of Jacques Guillemeau, *Child-birth, or the Happy Deliverie of Women* . . . London, A. Hatfield, 1612. The author, a physician and gynaecologist of great repute, was in the service of Charles IX, Henry III and Henry IV.

The large collection of books on foods and cookery given to this Library by Dr. Margaret Barclay Wilson was augmented by sixty-nine books, and she presented in addition 3,101 numbers of unbound medical journals. Among her recent gifts may be mentioned: Marsilius Ficinus, *De Vita Libri Tres,* Basileae, 1541, a popular work on diet and hygiene by a fifteenth century physician; Thomas Hall, *The Queen's Royal Cookery,* London, ca. 1734; and Apicius, *De Opsoniis et Condimentis,* London, 1705, an edition of the most famous of cook-books, edited by the zoologist and author, Martin Lister.

Two beautifully printed modern books were welcome gifts. One, presented by Mr. William B. Osgood Field and compiled by him, is entitled *John Leech on my Shelves,* privately printed by the Bremer Presse, Munich, in 1930. It will be remembered that Leech studied medicine before devoting himself to art. The other modern edition referred to above was printed for Mr. William Andrews Clark, Jr. and donated by him. It appeared in two volumes, one a facsimile of Robert Louis Stevenson's *Father Damien: an Open Letter to the Reverend Dr. Hyde of Honolulu,* Sydney, 1890; the other a modern printing of the same letter with copious notes by Mr. Clark on the life of the priest who dedicated his life to service among the lepers. These two volumes appeared together in 1930.

Our Americana collection was enriched by a gift of Dr. Ignac Neumann: *An Abstract of the Patent granted by His Majesty King George to Benj. Okell, the Inventor of a Medicine, call'd Dr. Bateman's Pectoral Drops* . . . New York, John Peter Zenger, 1731. The name of the printer

of this valuable little document is associated always with the struggle for the freedom of the press in this country. We are indebted to Dr. F. M. Al-Akl for an interesting group of Chinese medical charts, books and instruments, left here on permanent loan. The addition of records and minutes of medical societies is always desirable. The West Side Clinical Society were kind enough to add the minutes of their society to those already on our shelves. Other manuscript material was contributed by Dr. Mary E. Jarvis, who presented military diaries and notes of frontier service of her father-in-law, Dr. Nathan S. Jarvis, Sr., and certificates, commissions and notes on an expedition to the Grand Cañon in 1887-8, of her late husband, Dr. Nathan S. Jarvis, Jr.

Among the many advantages of the new Academy extension, not the least is the provision of ample and appropriate space for the housing and display of medical instruments, specimens, models, etc. We were very happy this year to receive from Mr. Alfred F. W. Seaman some instruments belonging to Valentine Seaman which were said to have come to him from Edward Jenner. A gift of considerable interest presented to the Academy by Guy's Hospital, consists of sections cut from the three remaining kidneys which originally were in the possession of and were described by Dr. Bright. Room in the new building was provided, too, for our art collection, which comprises original work done by medical men, as well as photographs, portraits, etc. Seven etchings done by Dr. Arpad Gerster were recently given by Dr. Samuel W. Lambert. During the recent exhibition in honor of William Beaumont, Dr. Irving Pardee presented a daguerreotype and silhouette of the army surgeon who did so much for the physiology of digestion.

We would like to make special mention of two large donations of good standard medical books: Dr. Theodore H. Allen's, amounting to 1069, and Dr. Sachs' of 313.

Purchases

In a time when funds are scarce and currency is fluctuating, we do not expect to fill many gaps in our collections and lessen the number of our desiderata. We were, therefore, more than pleased this year to acquire through the Rare Book Fund a copy of the first German translation of Realdus Columbus' anatomy which was published by Theodore de Bry in 1609. The anatomy itself is a work we are glad to possess, but our eagerness for the volume was chiefly because of its appendix which contains Volcher Coiter's famous plates of zoological comparative anatomy. They are exact copies of the excessively rare first edition, Nürnberg, 1575, which is considered the first important work in comparative anatomy. Bound with it is a copy of Fabricius de Aquapendente's *De Visione, Voce, et Auditu*, Frankfort, de Bry, ca. 1605. The binding of full brown morocco bears the arms and initials of Ferdinand, Archduke of Austria and the date, 1609. Another important item we were able to buy is the *Anatomiae, sive de Resolutione Corporis Humani* . . . of Costanzo Varolio, published in Frankfort in 1591. Although this is the first edition of the *Anatomiae*, it includes the second printing of *De Nervis Opticis*. The latter appeared first in 1573, and the author describes the crura, the commissure and the pons.

Among the sixteenth century books which we purchased are: Matthias Cornax, *Medicae Consultationes . . . Enchiridion*, Basileae, per Ioannem Oporinum [printer of Vesalius], 1564; Michael Scotus, *Physionomia*, Vinegia, Melchior Sessa, 1530, an early Italian translation of the tract which in spite of its title deals mostly with the process of generation; Thomas Erastus, *Varia Opuscula Medica*, Francofurdi, apud Ioannem Wechelum, 1590, an author known for his controversial writings in medicine and theology; a polyglot edition of the popular tract on personal hygiene, *Regimen Sanitatis* of the School of Salernum, printed in Cracow in 1543 in Latin, German and Polish. The Library was fortunate also in the purchase of another edition of the *Regimen* in English, London,

Wyllyam How for Abraham Veale, 1575. In 1582 appeared *Batman uppon Bartholome, his Booke De Proprietatibus Rerum*, London, imprinted by Thomas East. An English translation of the encyclopaedia of the Middle Ages by Bartholomaeus Anglicus was printed about 1495. A copy of the 1582 translation of Stephen Batman, Chamberlain of Queen Elizabeth's household, has recently been added to our list of English books printed before 1641. The brilliant seventeenth century scientist, Francesco Redi, was the author of a history of the invention of eyeglasses, which was published first in 1678. The edition which the Library now possesses is that of Firenze, 1690, entitled *Lettere intorno all' Invenzione degli Occhiali*.

We are always happy to place upon our Americana shelves theses published in the eighteenth century by American medical students in the universities abroad. A recent accession is the dissertation of Ephraim Howard, *De Variolarum Insitione*, Leyden, 1767. Howard practiced medicine in Elkridge, Maryland, and served as a member of the State Convention in 1774. The first edition of Dr. John Aikin's *View of the Life, Travels, and Philanthropic Labours of . . . John Howard*, came out in 1792, two years after the latter's death. In 1794 two American editions appeared. For some time the Academy has had a copy of the Philadelphia edition, and this year we placed beside it a copy of the one printed in Boston. John Howard is remembered for his achievements in the reform of sanitary conditions in prisons and hospitals. Alexander Anderson's memory has been kept alive, not because of his eminence as a physician, but rather on account of his skill as a wood engraver. Added to our growing collection of manuscripts this year was his license to practice medicine in New York in 1795. We were fortunate also in obtaining as a gift from Mr. Odell D. Tompkins, Dr. C. L. Dana's own copy of his book, *Poetry and the Doctors*, with annotations in his hand for a contemplated enlarged edition. Supplementing this we bought a letter from Sir William Osler to Dr. Dana, praising the book and making suggestions to be incorporated in any future edition.

Exhibitions

Although recent acquisitions will be displayed from time to time in the small cases designed for that purpose in the Rare Book Room, it is our intention to continue having exhibitions of books in the centre of the Reading Room on the third floor or in the Collation Room on the first floor. During the last year an elaborate exhibition was prepared in honor of the one hundredth anniversary of the publication of William Beaumont's book on the physiology of digestion. Dr. Harris A. Houghton, who was chairman of the committee in charge of the celebration, was responsible for the assembling of material, much of it difficult to locate and sought from interested admirers of Beaumont throughout this country. This opened on October 5th and remained on view until the end of the Graduate Fortnight. A small exhibition of books on metabolism was arranged by Dr. Eugene F. Du Bois in connection with the Fortnight.

Library Publication Fund

Through the good offices of Dr. Samuel W. Lambert, a member of this Committee, one of the Library's warmest friends, we are able to record generous donations amounting to $8,250 (in addition to $5,000 received in 1932) towards the Publication Fund. Work is progressing steadily upon the atlas of Vesalian illustrations, containing several hundred fresh woodcuts made from the original woodblocks after drawings by Jan Stephan van Calcar. These blocks were found in the Munich University Library. The printing and making of this atlas have been entrusted to Dr. Willy Wiegand of the famous Bremer Presse of Munich, and the result will be a very beautiful work of great value to all interested in the history of anatomy and anatomical illustration. It is believed that the atlas will be on sale before the end of 1934. A vote of thanks and appreciation to Dr. Lambert was tendered by this Committee for the success of his efforts.

MISCELLANEOUS

From the minutes of this Committee it is possible to make notes of some of its activities and of the varied topics it has discussed. For some time it has been thought that the Academy might be of great service, if funds were available, in establishing branch libraries or aiding libraries in the boroughs of the Bronx, Queens, and Richmond. Money is not to hand, but a rough plan for future action has been drawn up and the matter was talked over with those in the Bronx and Richmond interested in such a scheme. For some years now we have been in the habit of turning over many duplicate textbooks to the Queens Academy of Medicine and to several hospital libraries.

The American Medical Association has had to reduce the number of medical periodicals which it indexes. A conference was arranged and held in January. It was attended by Dr. Morris Fishbein, editor of the *Quarterly Cumulative Index Medicus,* your Chairman and Dr. A. E. Cohn, and by the Librarian, Miss Doe (the Assistant Librarian) and Miss Wilson who is in charge of the Periodical Department. It was pointed out to Dr. Fishbein that now there is a good deal of duplication of expenditure and effort, owing to the fact that about a thousand medical magazines are being indexed at one and the same time: at Washington for future volumes of the *Index Catalogue of the Surgeon General's Library* and at Chicago for the *Quarterly Cumulative Index Medicus.* Dr. Fishbein promised to see what he could do about the matter, and letters were written to the Army Medical Library on the same subject. The Cataloguing Department of this library now makes cards for all or some of the articles in twenty-nine periodicals which are not indexed for the *Quarterly Cumulative Index Medicus,* and has also catalogued the articles in many Handbücher and systems of medicine, etc. Several journals have been lent to the American Medical Association to be indexed.

This Committee congratulated Dr. B. W. Weinberger, the Consultant in Dental Bibliography, on the publication

of the second part of his *Dental Bibliography,* which is "a reference index to the literature of dental science and art as found in the Libraries of the New York Academy of Medicine and Bernhard Wolf Weinberger," published in New York, 1932. It might be added that, in Dr. Weinberger's opinion, the Dental Library of the Academy is the most complete in the world. That is, of course, supported by an annual grant from the First District Dental Society.

For the convenience of readers in consulting the volumes of the *Index Catalogue* and the *Quarterly Cumulative Index Medicus*, two sets of these publications have been arranged on tables in the room on the third floor which used to be the Rare Book Room. This facility has proved to be very acceptable.

The report of the voluntary workers on the Committee on Evaluation of Sex Literature presented by Mrs. Burchard Dutcher was received and thanks expressed for their valuable work.

For the exhibition held at the annual meeting of the American Medical Association at Milwaukee the Academy lent a group of books illustrating the history of urology. After the exhibition, the books were shown for a week in Chicago by the American Urological Society.

To reduce the expenses of binding this Committee agreed to the sewing-together of the separate numbers of about 200 magazines as a temporary measure.

The rising cost of many of the German scientific periodicals has been felt throughout the world, and many libraries have been faced with the possibility of cancellation. The Medical Library Association took concerted action, and the subject of these German periodicals was discussed by this Committee at several meetings. As the result of the joint efforts of the Medical Library Association and the American Library Association, we are happy to report that, at the Chicago meeting of the American Library Association in October, Dr. Ferdinand Springer, of the firm of Julius Springer, agreed to a 30 per cent reduction, for the first six

months of 1934, of the price of periodicals which cost more than forty dollars in 1932, and to a 40 per cent reduction of the price of two other very expensive periodicals. In addition Dr. Springer promised to reduce the price further in the second half of 1934.

This year, letters were sent out from the Periodical Department to all American Foundations which give funds for medical purposes, requesting complete files of their annual reports.

Volunteers

Our warmest thanks are due to the following volunteers for their good work in the Library during the year: Miss Martha Lambert has continued as a half-time volunteer in charge of the cataloguing and care of portraits; Mrs. Clay as a half-time volunteer, has catalogued books in the Rare Book and History Department during this autumn; Mr. Edward Orestuk and Mr. Edward Lonergan helped the pages as half-time workers for several weeks, thus training themselves for work in the library of the Seaview Hospital; Miss Eleanor MacHaffie for three weeks typed cards for the catalogue in the Rare Book and History Room; Miss Adelaide Neuburger worked two mornings a week for three months in the Periodical Department writing requests for hospital reports and checking donations; Miss Virginia Rodgers copied catalogue cards on a half-day basis, three days a week for a month and a half; Miss Florence Deutsch worked for half a day three times a week for three weeks copying catalogue cards; and Miss Sara Welcher worked for half a day three days a week for five weeks copying cards in the Catalogue Department. In addition, two workers were paid by the Emergency Work Bureau: Miss Ethel Sacks four days a week for six weeks for typing cards in the Rare Book and History Department and Miss Helen Welstead doing similar work for six hours, two days a week for three and a half weeks.

Periodicals and Modern Books

It was the opinion of this Committee that despite the decreased budget for Library expenses, subscriptions to periodicals should be maintained. On the other hand, very little money was spent on completing back files of magazines, although several sets, on order from previous years, were purchased. It will be seen from the statistical or tabular part of this report that only 2,665 purchased books and bound periodicals were accessioned whilst the number for 1931 was 4,552. In our prosperous days about two-thirds of all the new medical works were purchased, but in the autumn of this year, in considering 484 books (nearly all newly published), only 51 were bought.

Statistics for 1933

Donations

Publishers who have presented complimentary volumes:

D. Appleton-Century Company	8
Commonwealth Fund	1
F. A. Davis Company	1
Funk & Wagnalls Company	1
Ginn & Company	1
Paul B. Hoeber, Inc.	9
Lea & Febiger	13
Oxford University Press	17
W. B. Saunders Company	30
Charles C. Thomas	1
Williams & Wilkins	1
William Wood & Company	2

Donors of twenty or more volumes:

Mrs. Isador Abrahamson	85
Dr. T. H. Allen	1069
Dr. Moses Aronson	50
Dr. Martin Burke	63
Dr. J. K. Erganian	36
Mrs. Rolfe Floyd	400
Dr. L. F. Frissell	82
Dr. B. W. Hamilton	87
Dr. L. I. Harris	64
Dr. R. S. Haynes	46
Dr. A. F. Hess	26
Lenox Hill Hospital	94
Estate of Dr. John Leshure	53
Dr. R. L. Loughran	33
Mead Johnson & Company	27
Municipal Reference Library	35
New York Public Library	120
Committee on Costs of Medical Care	45
Rockefeller Foundation	231
Dr. J. C. Roper	23
Dr. Bernard Sachs	313
Dr. E. F. Traub	20
University of Wisconsin Medical School Library	20
Dr. M. B. Wilson	69
Woman's Hospital, City of New York	269
Dr. F. C. Yeomans	45

Donors of large numbers of unbound journals:

Dr. Isador Abrahamson	240
American Journal of Cancer	334
Archives of Pediatrics	486
Dr. S. T. Armstrong	226
College of Physicians & Surgeons	590
Dr. E. H. L. Corwin	504
Dr. A. B. Duel	219
Dr. J. K. Erganian	877
First District Dental Society	292
Dr. W. C. Fischer	221
Dr. A. A. Goldbloom	389
Dr. L. I. Harris	761
Dr. J. A. Hartwell	406
Dr. W. A. Heckard	214
Dr. A. W. Herzog	420
Dr. A. B. Hirsh	723
Dr. S. E. Jelliffe	266
Dr. Emmanuel Jonessoff	260
Dr. F. A. Kassebohm	429
Dr. S. A. Knopf	371
Life Extension Institute	292
Dr. W. J. Mersereau	482
Dr. Michael Michailovsky	306
Municipal Reference Library	484
New York Public Library	686
New York Telephone Company	359
Dr. R. Ottolengui	751
Dr. W. H. Park	344
Rockefeller Foundation	2324
Rockefeller Institute	242
Martin H. Smith Company	853
Dr. E. C. Titus	475
Dr. B. W. Weinberger	414
Dr. I. S. Wile	212
Dr. L. R. Williams	705
Dr. M. B. Wilson	3101
Dr. S. J. Woolley	320

Summary of donations:

Books	3,958
Journals	26,602
Pamphlets	14,355
Total	44,915

Donors of money:

Mrs. W. M. Brickner	$ 150.00
Carnegie Corporation	26,250.00
First District Dental Society	500.00
Dr. S. W. Lambert,	200.00
Mrs. Stafford McLean	10,000.00
Various donors to the Publication Fund (in addition to $5,000 in 1932)	8,250.00
Mr. and Mrs. Henry Wittkowski	10.00

Miscellaneous donations:

Dr. F. M. Al-Akl	Three Chinese charts (points for acupuncture-lateral view; points for acupuncture-dorsal view and human anatomy), Mongolian Book of Recipes, Tibetan Medicine and Prayer Book,

	native Chinese surgical instruments bought in Pekin in 1932 and one medical volume. These are on permanent loan.
Dr. Reginald Burbank	A certificate of membership in The New York Medical Academy, July 4, 1831.
Mr. T. H. Burch, Jr.	A large number of surgical instruments.
Dr. Martin Burke	An examination table, one chair, one battery and surgical instruments.
Dr. Isak Collijn	Facsimile of John Arderne, *De Arte Phisicali et de Cirurgia.* One of a hundred copies issued by the Kungl. Biblioteket, Stockholm, Sweden.
Mr. A. B. Comer	An amputation knife used by Dr. Alexander T. Comer during the Civil War when he was assistant surgeon of the 9th New York Cavalry.
Dr. F. S. Dennis	Bound manuscript of notes of surgical clinics of von Langenbeck, Surgeon-General of the Prussian Army, manuscript autographed by von Langenbeck. Notes taken by Dr. F. S. Dennis during the winters of 1876-1877 in Berlin.
Dr. R. L. Dickinson	Historical gynaecological instruments.
Mrs. H. R. Durfee	A daguerreotype (Dr. Bliss?).
Dr. A. B. Hirsh	A genito-urinary chart.
Mr. A. B. Horn	An engraving of Dr. Thomas Cullen.
Dr. John Horn	An otoconcussor and one autoscope. Records of operations, St. Mary's Hospital, Brooklyn, by Dr. John Horn, House-Surgeon, 1885-1886.
Mrs. M. D. Hopkins	A Hopkins chart, temperature and bedside notes.
Dr. M. E. Jarvi	Two manuscripts by Dr. Nathan S. Jarvis, Sr., Capt. U. S. Army. Manuscript and a book by Dr. Nathan S. Jarvis, Jr. Five certificates, appointments to rank of Major of Dr. N. S. Jarvis, Jr. in both the U. S. Army and National Guard of New York State. A diploma issued to Dr. Mary E. Jarvis,

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course in Public Health. Eight letters and engraver's plate for calling cards "Major N. S. Jarvis, U. S. Army, Retired." New York University matriculation tickets, 1819-1821. World War Service and other army papers. Manuscript of a biography of Dr. William C. Jarvis. *New York Journal of Medicine* for March 1847, containing an abstract of a letter from Dr. N. S. Jarvis, Surgeon, U. S. Army. A number of caricatures. Manuscript of a "Night of Terror" by Surgeon N. S. Jarvis, U. S. Army. Manuscript letters, 1812-1813 and Oct. 10, 1833. Twenty-seven diplomas, society certificates and army appointments.

Miss Florence Keen................Typescript of an address given by Dr. W. W. Keen at a dinner in honor of his eighty-fourth birthday.

Dr. S. W. Lambert..................Seven etchings by Dr. Arpad Gerster.

Dr. Morris Leff .... Fifty-six packages of blank slips for use by readers at reference tables.

Dr. Howard Lilienthal .... Report of a Committee of the Medical Society of the City and County of New York, appointed to investigate the subject of a Secret Medical Association, 1831. A letter of recommendation signed by A. D. Wilson, M.D.

Dr. F. E. MacLoghlin............. . "Influenza," a symphonic tone-poem.

Dr. Ignac Neumann.................A folder of manuscripts, among them notes on lectures, letters, photostats of diplomas. The manuscript of a charge delivered to graduates in medicine, at a commencement held at the College of Philadelphia, May 1, 1773. . . . *An abstract of a patent granted by His Majesty King George to Benj. Okell,* 1731, a short treatise on the virtues of Dr. Bateman's Pectoral Drops. Two note-books on the lectures of Valentine Mott. An old book of Evert Bancker, 1746, used by his grandson, George B. Bancker, ledger A commenced July 12th, 1803.

Periodicals

Journals:

	Subscriptions	Exchange or Gratis	Total
1. American	193	438	631
2. Belgian	12	7	19
3. British (except Canadian and Indian)	145	46	191
4. Canadian	6	21	27
5. Chinese	2	2	4
6. Dutch	15	9	24
7. French	163	31	194
8. German (including Austrian)	319	6	325
9. Indian (Asia)	9	11	20
10. Italian	114	33	147
11. Japanese	5	36	41
12. Portuguese (a) Portugal	1	4	5
(b) Brazil	2	20	22
13. Russian	8	4	12
14. Scandinavian	35	7	42
15. Spanish (a) Spain	15	16	31
(b) South America	5	53	58
16. Swiss (including League of Nations publications)	13	4	17
17. Miscellaneous (Czech, Greek, Hebrew, Hungarian, Polish, Rumanian, etc.)	5	41	46
Total	1,067	789	1,856
Total in 1932			1,934
Total in 1931			1,992
Total in 1930			1,965
Old titles of which no 1933 numbers have been received			185
New titles added in 1933			99

Summary of serial publications:

Journals received regularly	1,856
Journals received irregularly (by donation)	273
Annuals (reports of health departments, catalogues of medical ... £. S. etc.)	431
rts (annual administrative reports)	185
Mr. O. D. Tomp. kly, monthly, and quarterly health department	115
	2,863

Exchanges:

432 copies of the *Bulletin* are sent in exchange for 472 publications of other institutions (The difference between these and the 1932 figures is due to a drastic curtailment of our mailing-list for economic reasons.)

86 copies of the *Annual Report* are sent in exchange for the reports of a like number of institutions

Circulation Outside

	Books	Pamphlets	Journals	Borrowers
1925	3,181	1,319	3,708	713
1926	2,453	909	2,825	629
1927	3,178	1,104	3,764	765
1928	3,010	1,014	4,123	733
1929	2,772	872	4,228	765
1930	3,697	1,032	4,915	884
1931	4,453	1,027	6,147	968
1932	5,012	1,131	7,291	993
1933	5,354	1,043	6,491	1,047

Circulation Inside

Books, journals and pamphlets from stacks used in Reading Rooms

1933	81,475 items

Interlibrary Loans

1930	637 books to 57 libraries
1931	820 books to 80 libraries
1932	1,322 books to 89 libraries
1933	2,089 books to 129 libraries

Readers

	Total number of readers	Holidays and Sundays
1925	33,425	708
1926 (moving)	22,350	613
1927	26,093	1,135
1928	29,239	1,519
1929	31,180	1,437
1930	37,539	1,558
1931	40,412	1,408
1932	47,042	1,716
1933	45,031	1,800

Finance

Binding (2,241 books)	$ 3,988.25
Periodicals	12,070.22
Completing files	466.29
Books (including $516.04 for Rare Books)	3,835.61
Miscellaneous	4,712.78
Salaries	54,351.60
Total	$79,424.75

Bibliographical Department

	Pieces of Work	Bibliographies Made	Income
1929	396	98	$3,921.98
1930	365	89	3,819.37
1931	409	76	4,547.70
1932	352	97	3,793.17
1933	315	44	2,705.77

(In 1933 one member of the staff was transferred to another department)
Considerable work is also done for other Academy departments, for which no charge is made.

Photostat Department

	Pieces of Work	Income
1929	531	$1,871.13
1930	535	1,995.11
1931	538	1,828.11
1932	531	1,425.75
1933	625	1,537.03

Considerable work is also done for other Academy departments, for which no charge is made.

Theses

	Catalogued	Cards sent to Columbia University
Prior to 1930	14,587	
1930	2,500	5,500
1931	2,367	2,758
1932	3,785	2,240
1933	7,270	4,271
Total	30,509	Total 14.769
Not yet catalogued	29,496	
Grand Total	60,005	

Disposal of Duplicates

	Receiving libraries, etc.	Bound vols.	Unbound jour.	Theses
1930	90	1,619	9,122	
1931	71	1,446	6,727	
1932	65	2,128	6,262	5,129
1933	78	1,611	3,258	825

Miscellaneous

	1929	1930	1931	1932	1933
Items repaired	8,474	7,093	6,692	7,715	6,842
Library-cards issued	1,108	1,212	1,376	1,665	1,563
Library subscriptions (total)	28	30	22	30	25
Library subscriptions renewed		16	13	12	17
Messenger deliveries for Fellows			312	277	383
Messenger deliveries (total)			1,269	1,246	1,121
Portraits (separate) catalogued					807
Portraits (in books, etc.) catalogued					3,395

Miss Doe, Assistant Librarian, represented the Academy at the Annual Meeting of the Medical Library Association held in Chicago, 19-21 June. The Librarian has been appointed a member of a committee of advisers to, and consultants with, the Army Medical Library.

By a change in the Constitution of the Academy, the Committee on Library has been increased from five to nine members; membership is to last three years; three members are to be elected and three to retire each year.

We are much indebted to Dr. Robert L. Dickinson, a Fellow of the Academy, for his drawings of the Rare Book and History Room.

J. Ramsay Hunt, *Chairman.*

REPORT OF THE COMMITTEE ON PUBLIC HEALTH RELATIONS

The following is a brief account of the activities of the Committee on Public Health Relations for the year 1933.

Maternal Mortality

The report, based on a study of 2,041 deaths which occurred in three years, 1930, 1931 and 1932, was published during the year by the Commonwealth Fund, which financed this study. All the facts ascertained during the course of the study were subjected to a searching scrutiny and the report brings out in full detail the ways and means of improving the present situation relative to the obstetric care of a very large part of our city population. The findings of the study have given impetus to endeavors on the part of medical, teaching and social welfare organizations for the improvement of existing conditions.

Diabetes

The statistical and preventive aspects of the problem of diabetes were a subject of a special study and report. Although the death rate from diabetes per 100,000 population is an unreliable and crude measure of the prevalence of the disease, the indications are that in New York City diabetes may not be on the increase; its prevalence, however, is considerable and probably exceeds that of tuberculosis. The report stresses the fact that modern methods of treatment, when intelligently and conscientiously applied, not only remove the immediate dangers of the disease, but serve to retard, if not to prevent, the later effects (especially arteriosclerosis, infections and gangrene), and thus make it possible for many diabetic individuals to live out their natural span of life.

Among the recommendations made for the provision of a uniformly high grade of treatment are: the coordination of the present postgraduate courses in the management of diabetes so that they will not overlap one another and will be available to the practicing physicians at all times, and

the establishment of an Association of Diabetic Clinics for the maintenance of uniformly high standards and for the dissemination of information to the public with regard to the prevalence of the disease and its amenability to proper treatment. In cooperation with the New York Tuberculosis and Health Association steps have been taken toward the formation of such an association.

Diabetes was made the subject matter of the Biggs Lecture for 1933.

AMOEBIC DYSENTERY

The increase in the number of cases of amoebiasis in New York City in the autumn of 1933 was the cause of a special inquiry into the problem from the preventive as well as curative aspect of it. The recommendations of the Committee were submitted to the health authorities of the city, and the policy pursued by the Health Commissioner was in accordance with the recommendations made in the report.

MEDICAL SERVICES FOR CITY EMPLOYEES

The organization and scope of the several medical services in the city for the health protection and medical care of city employees was a subject of special study. Existing practices and regulations relative to sick leaves were taken up in conjunction with this study and a report on this subject is being prepared.

THE WORKMEN'S COMPENSATION SERVICE FOR CITY EMPLOYEES

The City of New York is a self-insurer insofar as liability under the Workmen's Compensation Act is concerned. This activity is a part of the functions of the Corporation Counsel. In cooperation with the Mayor's Citizens' Committee, a study was made of the organization and mode of operation of this service. A report on the study together with the recommendations relative to this branch of municipal activity was submitted to the City authorities.

City Budget

The annual studies of the budgets of the City departments concerned with public health, hospitals and sanitation, were undertaken during the past year with the active participation of the Mayor's Citizens' Committee, as well as the Citizen's Budget Commission. The recommendations, carrying numerous suggestions for economies and changes, were submitted to the Mayor and the Board of Estimate, as well as to the Commissioners of the respective departments.

The Overcrowding of Municipal Hospitals

The financial situation in New York City has become too serious to permit overlooking the fact that drastic economies must be made in the conduct of our City affairs. In its communication to the City authorities the Committee stressed the need of efficient management but pointed out that economies in the departments dealing with the health and welfare of the community should not be made haphazardly. Only the relatively unessential positions and services should be curtailed or eliminated, and care taken that standards of medical practice, nursing and other auxiliary work be not lowered.

The City of New York owns and maintains 26 hospitals and institutions, of which 12 are general hospitals for acute and semi-acute conditions, with a bed capacity of 9,428; five are hospitals for communicable diseases, with a bed capacity of 1,900 beds. The total number of beds in the entire hospital system constitutes over one-third of the hospital bed capacity in the City.

Since 1930 there has been a steadily growing demand for accommodation in the municipal hospitals. While in 1929 the number of patient days in the municipal hospitals constituted 37.4 per cent of the total number of patient days in all hospitals in the City, it rose to 39.8 per cent in 1930, to 42.2 per cent in 1931, 42.3 per cent in 1932, and in the year 1933 it rose still further. It has not been uncommon to find forty patients cared for in a ward with a normal

capacity of twenty-five beds. A rise in demand of such proportions causes serious overcrowding and necessitates the placing of additional beds or cots in the middle of the wards, and even in the corridors. Overcrowding, aside from creating hazards to the health of the patients, throws an enormous burden on the physical facilities of the hospitals, and on the staff, and makes considerable additional demands on the food and supply budgets.

The Committee urged upon the Mayor and the Board of Estimate to make arrangements with the voluntary hospitals whereby patients applying to the municipal hospitals would be referred to other institutions and recognized as city charges.

Particular stress has been laid on the overcrowding of the maternity wards and attention called to the need of a change in the regulation to make possible the payment by the City for the confinement of indigent women when they have received prenatal instruction in the voluntary hospital in which they were delivered. Payment for indigent patients in voluntary hospitals is certified only when the patients are received as "emergencies," and in case of childbirth a case is considered as "pre-arranged" if the woman has received prenatal instruction. This rule has caused many of the patients to shun prenatal care, and the Committee feels that it is imperative for the City authorities to make a change in the regulation.

Cooperative Purchase of Hospital Care

The plan of pre-payment of hospital costs on a monthly basis, worked out by the Hospital Information and Service Bureau of the United Hospital Fund in cooperation with other bodies in the City, received a thorough study and critical analysis by the Committee. The fundamental principle of the proposal was endorsed by the Committee. When properly organized, the scheme may prove to be of considerable financial aid to the voluntary hospitals as it will change the status of many patients from the freeward to the semi-private category; and it may create an addi-

tional source of income to physicians who, at the present time, treat the majority of hospital patients without recompense. The plan provides for a free choice of physician by the patient and preserves the relationship of the family physician to patient throughout the period of hospitalization. It tends to bring all the voluntary hospitals together without in any way infringing upon any hospital's autonomy, and provides a means of partially distributing the cost of illness without invoking the instrumentality of state health insurance with all its political implications. In endorsing the general principles of the plan the Committee stressed the paramount importance of a proper set-up in order that untoward developments may be avoided and a high grade of medical service maintained in all hospitals in which the plan may be put in operation.

Legislation for the Control of Food, Drugs and Cosmetics

The attention of the Committee has been called to the need of strengthening the existing federal legislation to make it possible for the government to deal more successfully than has been possible under the present law, with false and fraudulent claims concerning the efficacy of many drug preparations; for the protection of food supplies; and for effective guarding against the employment of deleterious substances in cosmetic preparations. The public does not realize that such powerful drugs as thallium, pyrogallol, paraphenylendiamin, and salts of the heavy metals—lead, silver and mercury—may be elements in some of the cosmetic preparations. An added problem which affects the enforcement of the existing law and the protection of the public, is that many of the poisons used are so slow in revealing their effects that people do not associate the use of a medicine or of an application six months or a year before, with the appearance of symptoms of a chronic disease.

Impressed with the need of better provision for the protection of the public health, the Committee voted to support the so-called Tugwell Bill.

Housing

A great deal of attention has been given to the problem of housing. Conferences were held with experts in this line of work and certain legislative acts were endorsed and some were opposed by the Committee. The Committee opposed an amendment to the existing law permitting the continuance of occupancy of cellars in which over 20,000 families in this city are said to be still living.

The Committee urged the passage of an amendment to the Law, providing for a toilet for every family, and prohibiting the use of windowless rooms in old Law tenements after January 1, 1936.

Literature dealing with health aspects of the housing problem was examined and collated.

Socialized Medicine

Following the presentation of the report of the Committee on Costs of Medical Care, the various aspects of this problem were considered by the Committee at several meetings, one of which was attended by Dr. George F. McCleary, of London, former Principal Medical Officer of the National Health Insurance Commission, who visited New York, and who very kindly gave the Committee his views concerning the workings and effects of Health Insurance and Workmen's Compensation in Great Britain.

Veterans' Preference in Civil Service Appointments

The Committee has consistently opposed preferential treatment of all veterans in the civil service system. The practice whereby ex-service men are given preference over their fellow competitors, not only when they are first appointed, but in subsequent promotions, has done such serious harm to the civil service system as to constitute a menace to the morale of the entire service. It has brought

about the appointment and promotion of men of lesser qualifications at the expense of thousands who head the eligible lists.

The present veterans' preference system in New York State was incorporated in the State Constitution in 1929. It was intended to benefit those veterans who actually have a disability due to war service. In practice, however, many are certified by the Veterans' Bureau as disabled, who saw no war service and whose disability is often as negligible as to be rated at 1 per cent.

At the November elections in 1933, an amendment to the Constitution was submitted to the electorate providing for an extension of this privilege to veterans who were not citizens at the time of their enlistment in the service. The Committee joined with other organizations in protest against the re-ratification of the principle involved. The amendment was defeated.

Federal Economy Bill

One of the most important publications of the Committee in 1932 was the report dealing with the abuses connected with medical service under the Veterans' Relief Act. The Federal Economy Bill of 1933 contained provisions designed to curtail certain of the abuses pointed out in the Committee's report. The Bill was strongly endorsed by the Committee when it came up for consideration in the Congress.

Budget of U. S. Public Health Service

It was brought to the attention of the Committee that there was danger that the budget of the U. S. Public Health Service would be cut almost disastrously. It was also reported that the appropriation for the Research Laboratory of the Service was to be cut from $380,000 to $55,000. The Committee entered a protest with the Director of the Budget against this crippling of the U. S. Public Health Service which would have necessitated the curtailment of many valuable and vital activities.

Mid-Decennial Population Census

In view of the population movements which have taken place in this country as a result of the economic upset, the estimates of morbidity and mortality, as well as of other important economic and sociologic phenomena, such as dependency, delinquency, crime, per capita expenditures of public funds, etc., have become utterly unreliable. The period of ten years intervening between censuses is now recognized as too long for reliable population estimates and some foreign countries have adopted the quinquennial period for population enumerations. Estimates of the population by school registration figures in New York City in 1933 show a decline since 1930, whereas arithmetical progression shows an increase of about 415,000. It is the opinion of expert statisticians that there are no reliable ways of estimating fairly accurately the population except by a house-to-house census canvass. In view of this the Committee passed a resolution urging upon the Federal authorities the undertaking of a mid-decennial population count.

Control of Proprietary Hospitals

There are in New York City at the present time 107 proprietary hospitals (only three of which are on the approved list of the American College of Surgeons) with a total capacity of 3,454 beds and 1,276 bassinets. During 1933, 59,553 patients were treated in these hospitals. These institutions were formerly under the control and supervision of the Department of Health. Since the organization of the Department of Hospitals in 1929, this jurisdiction was transferred to the newly created Hospital Department. Rules and regulations have been promulgated dealing with requirements for plant equipment, administration and keeping of records. All permits are issued on an annual basis.

In order to eliminate certain reprehensible practices, an association of these hospitals has been created for the purpose of self discipline, but only fourteen hospitals are

members of this association. The Bronx County Medical Society has made certain arrangements with the proprietary hospitals of that Borough with a view of eliminating rebates. The situation, however, is not quite satisfactory and the matter of standards for proper control has been considered by the Committee for the purpose of making representations to the proper City authorities.

Miscellaneous

The numerous other activities of the Committee, for lack of space, must be merely enumerated. Among these should be mentioned the formulation, at the request of Mr. Harry L. Hopkins, of a policy concerning the medical aspects of public relief in this city for the guidance of the New York State Temporary Emergency Relief Administration; the Health Department requirements relative to the control of private clinical laboratories; dispensary practice and laws designed to eliminate the alleged abuses; the need of a study of the so-called marriage consultation bureaus which are scattered throughout the country, with a view of obtaining information concerning the methods of procedure, the extent and character of the demand made upon them, and the results of their activities.

The Committee arranged for a course of lectures in Industrial Hygiene similar to that of the year before; undertook the preparation of a schedule for the systematic study and appraisal of hospitals by the Hospital Information and Service Bureau of the United Hospital Fund; took up anew the problem of smoke abatement and the question of prevention of asphyxial deaths. The truancy problem as well as the existing provision for convalescent care of children and adults were subjects of inquiry.

As in the past years, the Committee was called upon to deal with various legislative measures affecting the public health, the hospitals and scientific research.

James Alexander Miller, *Chairman.*

REPORT OF THE COMMITTEE ON MEDICAL EDUCATION

Training of Interns and Specialists

A final report, which included important recommendations, was submitted to the Council of the Academy in January. Continuation of the study will be undertaken by a group called the New York Committee on the Study of Internships and Residencies. This group is composed of the Deans of the five medical schools of the city and five Fellows who represent the Academy.

Trends in Medical Practice

In January the Council asked the Committee to undertake a study of the Report of the Commission on Medical Education and to make recommendations. In starting the work the Committee decided to study at the same time two other reports which bear upon trends in medical practice—the Report of the Committee on the Costs of Medical Care and a Report on Hospital Service recently prepared by a member of the Committee. The Sub-Committee recommended that Dr. Henry E. Sigerist, Professor of the History of Medicine, Johns Hopkins University, be invited to deliver a special lecture at the Academy on the "Historical Background of Social or State Medicine." The lecture was delivered on October 25th, and attracted a large audience. At the December meeting of the Committee, an Ad Interim Report was presented outlining the results of the study to date.

Opportunities for Postgraduate Medical Study in New York City

The Committee has continued its survey of postgraduate medical education in New York with a view to improving the value of existing opportunities and encouraging the development of additional ones. Approval is given to those opportunities which after investigation have been found to be well organized with adequate equipment and clinical

material and given by physicians of character who are known to be qualified teachers in their special lines of work.

The result of each year's survey is published in the form of a synopsis which is widely distributed.

It has been found that short courses offered in the different institutions are decreasing in number while the longer courses, comprehensive in character, are increasing. Courses in the last named class are now offered in seven of the clinical branches.

The Daily Bulletin, which has been published since 1912, announces the operative work to be performed in the clinics of most of the important hospitals of the city, as well as the meetings, lectures, conferences and hospital rounds of the day. The requirements for posting provide that the clinician shall have met special qualifications in his line of special practice and also as a teacher, and that the hospital in which the clinics are given shall have been approved for teaching purposes.

The Bulletin of Non-Operative Clinics has been revised. It has been published in Medical Week and reprinted for general distribution. This Bulletin announces a total of 156 clinics in 23 special subjects, held in 33 hospitals of the city.

Bureau of Clinical Information

The Bureau has continued to serve as a clearing house of information in regard to opportunities for postgraduate medical study in this and other countries. The opportunities offered in New York City in the way of courses, clinics, conferences and hospital rounds are set forth in the bulletins and announcements published by the Committee.

Opportunities to follow the work of leading clinicians are effected by special arrangements with the clinicians concerned.

The Bureau is called upon to answer an increasingly large number of inquiries regarding medical matters of many kinds.

The number of out-of-town physicians who visit the Bureau has continued to decrease. During the year a total of 214 registered in the Bureau. Of these, 79 came from foreign countries.

Academy Programs

Meetings: The Program Committee with the cooperation of the officers of the several sections arranged the programs for the Stated Meetings of the year. The Program Committee also met with the Committee on Sections for a discussion of the scientific work of the Sections. The second Stated Meeting of each month has been presented by the Harvey Society. The program of the Annual Meeting was taken up with addresses of the retiring President and of the incoming President. At this meeting the Constitution and By-Laws of the Academy were amended so as to provide for the classification of Fellows and for a new class to be called Members. The Biggs Memorial Lecture of the year constituted the program of one Stated Meeting. The program of another Stated Meeting was presented by the Beaumont Celebration Committee. The Carpenter Lecture of the year was included in the program of the Graduate Fortnight. The Anniversary Discourse was delivered at the first Stated Meeting of November.

Lectures: The Eighth Series of Friday Afternoon Lectures on subjects of especial interest to the practitioner was arranged to include twenty lectures. The attendance at all the lectures was excellent and averaged over 250.

Several special lectures arranged by the Program Committee and by the Sections were given during the year. The programs of Stated, Section and special meetings as well as of lectures held under Academy auspices, are announced in the Academy Folder and are made of permanent record in the monthly Bulletin of the Academy.

Graduate Fortnight

The Sixth Annual Graduate Fortnight was held October 23 to November 3. The same features that had been presented in previous years were included in the program. The subject chosen was "Disorders of Metabolism." Fifteen hospitals cooperated in presenting afternoon clinics which dealt with various phases of the general subject. Ten evening meetings were held at the Academy, one of which was arranged in cooperation with the Medical Society of the County of New York.

For the first time a charge was made for attendance. Tickets of admission were issued without charge to Fellows of the Academy and to those who contributed to the program. A total of 643 physicians registered by paying the fee of two dollars. Complimentary tickets were issued to interns and residents, approved hospital fourth year medical students, medical officers of the government service, and a few dieticians and nurses.

The attendance at the evening meetings several times taxed the capacity of the hall. The smallest attendance was 448 and the average was 650, not including the meeting arranged in cooperation with the County Medical Society. At the last named meeting nearly 1,800 persons tried to hear the papers presented. On this occasion loud speakers were installed in two section rooms in anticipation of an overflow.

Interest in the clinics of the Fortnight appears to have been greater than that of previous years. All clinics were very well attended, the average attendance being about 160.

The scientific exhibit which was larger than any held heretofore filled the four large exhibit rooms in the new building, the collation room and the main hall. About 95 topics were exhibited by 160 exhibitors, 30 hospitals and several commercial organizations. An exhibit of books was arranged and the extensive exhibit of the Celebration of the 100th Anniversary of the Publication of William Beaumont's Book was held over during the period of the Fortnight.

Each evening special demonstrations, including presentations of fresh pathology, were held at 7:30 preceding the evening meeting. Also, demonstrations of individual exhibits were arranged at booths at fifteen minute intervals. The evening attendance at the exhibit averaged about 400 and the daily attendance over 1,000.

The Alexander Cochran Bowen Scholarships

The Bowen Scholarships provide for one year's clinical study abroad and are awarded to recent graduate interns from New York City hospitals which accept charity patients. The successful candidates of the year were Dr. Hollis L. Albright of St. Luke's Hospital and Dr. Milton Kissin of Beth Israel Hospital.

Bulletin of the Academy

The monthly Bulletin of the Academy (Second Series) is now in its ninth year of publication. Lack of funds prevents its enlargement as contemplated by the Committee and in consequence the size of the Bulletin has remained at approximately 64 pages. Proceeds from advertising now go far toward meeting the cost of printing.

The papers presented at the evening meetings of the 1933 Graduate Fortnight are being published in full in the Bulletin. A considerable increase in the number of subscriptions followed this announcement.

Miscellaneous

During the year the Committee has discussed and acted upon a number of questions referred to it by the Council. Recommendations were made in regard to the creation of new sections in Cardiology, Bacteriology, Immunology and Physical Therapy. A Sub-Committee reported on certain changes in the Pharmacopeia, and recommendations were made to the Council in the matter. A revision of the approved list of foreign clinicians is being undertaken. Some consideration was given to the use of the metric system in prescription writing but no action was taken.

In August occurred the death of Dr. Nellis B. Foster, a member of the Committee for eight years, and its Chairman for four years, 1928 to 1932.

HARLOW BROOKS, *Chairman.*

REPORT OF THE COMMITTEE ON SECTIONS

The average attendance at Section meetings during the year and the attendance during the two previous years are shown in the following table:

	1931	1932	1933
Section of Dermatology and Syphilology	123	122	95
Section of Surgery	92	102	137
Section of Neurology and Psychiatry	199	280	160
Section of Pediatrics	165	169	164
Section of Ophthalmology	120	275	154
Section of Medicine	338	235	173
Section of Genito-Urinary Surgery	242	171	99
Section of Orthopedic Surgery	78	199	120
Section of Obstetrics and Gynecology	198	227	120
Section of Historical and Cultural Medicine	80	67	71
Section of Laryngology and Rhinology	160		
Section of Otolaryngology		184	129

The Committee on Sections, which is composed of the Chairmen of the scientific Sections of the Academy with one of the Vice-Presidents as its Chairman, has functioned in cooperation with the Program Committee. It has assisted the Sections and their Advisory Committees in planning programs for Stated Meetings of the Academy and in carrying on certain other Section activities.

FRED P. SOLLEY, *Chairman.*

REPORT OF THE MEDICAL INFORMATION BUREAU

During the calendar year of 1933, the Medical Information Bureau received and handled a total of 2571 inquiries.

Newspaper Inquiries

Twenty per cent, or 574, inquiries came from the newspapers. Practically every newspaper in Greater New York made use of the Bureau as a source of medical information, for review of medical news items received by them from other sources, for feature material and for advice on proffered advertisements of a medical or quasi-medical nature.

Associated Press Articles

During the year of 1933, the Bureau issued 313 daily columns to the Associated Press. They were published in approximately four-hundred newspapers throughout the country.

Medical Releases

The Medical Information Bureau issued thirty-three medical releases on important medical subjects. Included among these releases were the Presidential Address of the President of the Medical Society of the County of New York and the Thomas W. Salmon Memorial Lectures, the report on maternal mortality and abstracts of a number of the Graduate Fortnight papers.

Assistance to National and Social Health Organizations

During the year the Medical Information Bureau assisted a number of national and local public health organizations in promoting their educational activities. Notable among these were:

The National Tuberculosis Association
American Public Health Association
Tuberculosis & Health Ass'n of St. Louis
Metropolitan Life Insurance Company
New York Social Work Publicity Council

Social and Commercial Organizations

Seventy-six per cent (1971) of the total number of inquiries which the Medical Information Bureau received and handled came from:

social agencies / commercial agencies	399
individuals	397
doctors	404
miscellaneous	381
radio supervision	306
advertising agencies	17
consultants	67

The National Better Business Bureau presented twenty-one inquiries during the year.

Radio

Three-hundred-and-seventy radio talks were scheduled and delivered during 1933 under the supervision of the Medical Information Bureau. These talks were given over the major stations in New York City. Sixty-nine broadcasts were arranged for the Early Diagnosis Campaign in combatting tuberculosis and sixty-one during the Seal Sale Campaign. In this we had the cooperation of every tuberculosis agency. Throughout the year special broadcasts were arranged for the American Society for the Control of Cancer, United Hospital Fund, American Social Hygiene Association, First Institute of Podiatry.

The Academy Radio Hour

During 1933 Fellows of the Academy presented weekly addresses on timely medical subjects over WABC, which has a network reaching into practically every part of the country.

The Academy booklet "On the Air" giving instructions to doctors on the preparation of radio talks, has been reprinted by

The American Medical Association
The National Tuberculosis Association

The Academy received the cooperation and assistance of the New York Tuberculosis and Health Association in conducting its radio activities.

Annual Press Dinner

In June the Annual Press Dinner was held at the Academy of Medicine. Dr. Orrin S. Wightman, as in former years, generously served as host. The guest speaker of the evening was Dr. John H. Finley of the Times.

Cooperation With the Medical Society of the County of New York

Throughout the year the Medical Information Bureau has served the Medical Society of the County of New York in presenting its activities to the press.

The Bureau has continued to receive splendid cooperation from its consultants, of whom there are 107, representing 34 specialties.

John J. Moorhead, M.D., *Chairman.*

REPORT OF OFFICES AND MEETINGS AT THE ACADEMY

During the year the following organizations have maintained their offices in the Academy building:

American Otological Society, Inc.
Committee on Religion and Medicine
First District Dental Society
Medical Society of the County of New York
Medical Society of the State of New York
National Committee on Maternal Health, Inc.
New York Physicians Mutual Aid Association
New York Society for the Relief of Widows and Orphans of Medical Men
New York State Journal of Medicine
Society for the Prevention of Asphyxial Death

Meetings have been held in the Academy building by the following organizations:

American Academy of Pediatrics, Committee
American Hungarian Medical Association
American Otological Society, Inc.
American Society of Regional Anesthesia
American Society for the Study of Arthritis
American Urological Association, New York Society
Association of Hospital Social Workers
Association of Italian Physicians in America
First District Dental Society, General and Sections
German Medical Society
Harlem Dental Society
Health Education Lectures
Joint Diseases Hospital
Medical Association of the Greater City of New York
Medical Society of the County of New York, General and Committees
Medical Society of the State of New York, Committee
New York Academy of Pharmacy
New York Institute of Clinical Oral Pathology
New York Neurological Society
New York Physical Therapy Society
New York Society of Approved Roentgenologists
New York Society for Clinical Psychiatry
New York Society of Graduates in Medical Gymnastics and Massage
New York Society for the Relief of Widows and Orphans of Medical Men
New York Society for Thoracic Surgery
New York State Association of Occupational Therapists
New York State Society of Medical Masseurs, Inc.
New York Tuberculosis and Health Association, Committee
Pan-American Medical Association, New York Chapter
Society of Medical Jurisprudence
Society for Plastic and Reconstructive Surgery
Speedwell Society
Veterinary Medical Association of New York City
Women's Medical Association of New York City

Accommodations, free of charge, have been granted during the year to:

American Society for the Control of Cancer
Committee on Religion and Medicine
Harvey Society
Industrial Diseases Lecture
Manhattan State Hospital, Medical Board of Visitors
Milbank Memorial Fund, Conferences
National Conference on Nomenclature of Disease

New York Society for Experimental Biology and Medicine
New York Pathological Society
New York Roentgen Society
New York State Board of Medical Examiners, Medical Grievance Committee
Thomas W. Salmon Memorial Committee
Society for the Prevention of Asphyxial Death

OBITUARY 1933

FELLOWS

Abrahamson, Isador
Atkins, Richard T.
Barnum, Merritt Wright
Burch, T. Hamilton
Burke, Martin
Byrd, Charles Wise
Chapman, Charles F.
Clark, L. Pierce
Coffin, Lewis A.
Dixon, George Arthur
Farrington, William H.
Foster, Nellis Barnes
Frothingham, Richard
Girdner, John H.
Greene, Robert Holmes
Grout, Gerald H.
Hess, Alfred Fabian
Jarvis, Nathan S.
Kahn, Lipman Miller
Lane, John Edward
Lee, Burton J.
McCoy, John J.
Mortimer, W. Golden
Moschcowitz, Alexis V.
Nisbet, James Douglas
Norrie, Van Horne
Ochs, Benjamin F.
Peckham-Murray, Grace
Porter, William Henry
Rost, William L.
Schauffler, William G.
Stewart, George David
Swift, Edwin E.
Syms, Parker
Van Fleet, James Flandreau
Ward, Freeman Ford
Wolff, Henry A.
Wylie, Robert H.

ASSOCIATE FELLOW

Franken, Sigmund W. A.

HONORARY FELLOW

Roux, Emile

RECAPITULATION

Fellows 38
Associate Fellows 1
Honorary Fellows 1

FELLOWS, MEMBERS, ASSOCIATE FELLOWS AND ASSOCIATES ELECTED IN 1933

RESIDENT FELLOWS

Abeloff, Abram Joseph
Abramson, Harold
Ada, Alexander E. W.
Allison, Stanton T.
Altman, Harry S.
Andrus, William De Witt
Antopol, William
Astrachan, Girsch D.
Atwood, Edward A.
Baldwin, Francis W.
Berner, Frank
Bodo, Richard C.
Bosworth, David M.
Buchman, Joseph
Carroll, John
Christensen, Bryant E.
Co Tui, Frank
Dawson, Martin H.
Deery, Edwin M. G.
Druss, Joseph G.
Duryee, Abram Wilbur
Edlin, James S.
Eiss, Stanley
Ferraro, Armando
Foot, Nathan Chandler
Francis, Charles C.
Friedman, Benjamin
Goetsch, Arthur
Goldman, Irving Brice
Goldmark, Carl
Graham, Thomas Norris
Greene, Carl Hartley
Greenwald, Harry M.
Grethmann, Wolfgang
Hall, Henry Lawrence
Hallock, Leonard A.
Hanger, Franklin MacCue
Hanssen, Eilif C.
Harris, William
Heaton, Claude Edwin
Hennell, Herman
Heuer, George J.
Higinbotham, Norman L.
Hurley, Vincent
Jaffe, Henry Lewis
Johnson, Vansel S.
Kahle, Ralph Charles
Kelley, Eugene F.
Kereszturi, Camille
Kilroe, John Charles
Klingman, Walter O.
Kruna, Richard B.
Levy, David M.
Lilien, Adolph A.
Lisa, James R.
Livingston, Edward M.
Loth, Mathilde
Lowenfish, F. Philip
Lyons, L. Vosburgh
McConnell, Robert Hall
Marcus, Joseph M.
Marino, A. W. Martin
Mayer, Max David
Milici, Attilio
Miller, Charles S.
Miller, Julius A.
Moon-Adams, Dabney
Moyle, Eugene Henry

Neustaedter, Theodore
Niles, Henry D.
Opie, Eugene Lindsay
Pack, George Thomas
Pearce, Louise
Poltchaninoff, Nicholas J.
Pudney, William Kent
Rabiner, Abraham Max
Rosenthal, Theodore
Ryan, Charles Diller
St. George, Armin
Sanman, Louis F.
Savitsky, Nathan
Scarff, John Edwin
Selby, Nathaniel E.
Shoenfeld, Dudley D.
Sims, Charles Franklyn
Skeel, Henry Robertson
Sobel, Irwin P.
Solley, Robert Folger
Stoloff, E. Gordon
Summerill, Frederick
Taylor, John Arthur
Thompson, William P.
Tiebout, Harry Morgan
Tolmach, Jesse Alfred
Traeger, Cornelius Horace
Trubek, Max
Twiss, John Russell
Ulmar, David
Walzer, Matthew
Warbasse, James P.
Wertham, Frederic
Ziporkes, Joseph

Resident Members

Cipollaro, Anthony C.
Ginzburg, Leon
Grace, Arthur William
Martin, Hayes E.
Rappaport, Israel
Schwartz, Alfred A.

Non-Resident Fellows

Dalldorf, Gilbert J., Valhalla, N. Y.
Hirshfeld, Samuel, Los Angeles, Calif.
Ivins, William Clifford, Trenton, N. J.
Jameison, Gerald Reid, White Plains, N. Y.
Morgan, Audrey Goss, Washington, D. C.
Sprague, George S., White Plains, N. Y.
Steiner, Walter, Hartford, Conn.
Sutherland, Francis A., New Haven, Conn.
White, William Beverly, Stamford, Conn.

Associate Fellows

Berger, Adolph, New York.
Bouton, Clyde S., New York.
Dunbar, Helen Flanders, New York.

Associates

Bellows, Marjorie T., White Plains, N. Y.
Fischer, Robert Morris, New York.
Schweitzer, Jerome M., New York.

RECAPITULATION

Elected in 1933; Resident Fellows, 102; Resident Members, 6; Non-Resident Fellows, 9; Associate Fellows, 3; Associates, 3.

COMPLETE ACADEMY FELLOWSHIP

1933

RESIDENT FELLOWS

1913 Abbott, Theodore J.
1933 Abeloff, Abram Joseph
1901 Abraham, Joseph H.
*1910 Abrahamson, Isador
1917 Abramowitz, E. Wm.
1933 Abramson, Harold
1933 Ada, Alexander E. W.
1921 Adair, Frank Earl
1901 Adams, Charles F.
1905 Adams, Warren S.
1916 Addoms, Lewis P.
1909 Agatston, Sigmund A.
1907 Albee, Fred H.
1928 Aldridge, Albert H.
1905 Alger, Ellice M.
1920 Allen, Frederick M.
1931 Allen, Philip Daly
1930 Allen, Theophilus Powell
1929 Allison, Benjamin Roy
1933 Allison, Stanton T.
1911 Almgren-Dederer, Ebba E.
1928 Almour, Ralph
1930 Alofsin, Louis M.
1921 Altman, Emil
1933 Altman, Harry S.
1930 Amberson, J. Burns, Jr.
1915 Ames, Thaddeus H.
1915 Amey, J. Willis
1932 Amsden, George S.
1918 Amster, J. Lewis
1931 Andersen, Dorothy H.
1918 Anderton, Walter P.
1924 Andresen, Albert F. R.
1923 Andrews, George C.
1933 Andrus, William De Witt
1931 Anopol, George
1933 Antopol, William
1932 Apfelberg, Isidor
1932 Appelbaum, Emanuel
1909 Aranow, Harry
1918 Armstrong, Arthur S.
1924 Armstrong, Donald B.
1917 Armstrong, Edward McP.
1932 Arnheim, Ernest E.
1931 Arnowich, Julius
1928 Aronson, Louis S.
1889 Aronson, Moses
1913 Asch, Joseph Jefferson
1919 Aschner, Paul W.
1900 Ashley, Dexter D.
1928 Ashton, Leslie Orrel
1933 Astrachan, Girsch D.
1930 Atchley, Dana W.
*1921 Atkins, Richard T.
1898 Atkinson, James Wm.
1933 Atwood, Edward A.
1910 Auchincloss, Hugh
1912 Auerbach, Julius
1932 Auster, Lionel Sandler
1909 Avery, Oswald T.
1918 Babcock, James W.
1918 Baehr, George
1916 Bailey, Cameron V.

*Deceased

1901 Bainbridge, William Seaman
1918 Bainton, Joseph H.
1921 Baketel, H. Sheridan
1924 Bakwin, Harry
1933 Baldwin, Francis W.
1900 Baldwin, Helen
1927 Baldwin, Horace S.
1927 Balensweig, Irving
1907 Ballin, Milton J.
1914 Bancroft, Frederic W.
1914 Bandler, Clarence G.
1908 Bang, Richard T.
1924 Banowitch, Morris M.
1926 Barach, Alvan LeRoy
1914 Barber, W. Howard
1929 Barkhorn, Henry Charles
1930 Barnard, Margaret Witter
1930 Barnes, William J.
1908 Barringer, Benjamin S.
1908 Barringer, Emily Dunning
1924 Barrows, David Nye
1913 Barshell, Samuel
1930 Barthel, Else Anna
1909 Bartlett, Frederic H.
1899 Baruch, Herman B.
1913 Bass, Murray H.
1908 Bassler, Anthony
1914 Bastedo, Walter A.
1919 Bauman, Louis
1920 Beach, Bennett S.
1918 Bebb, Rose Anne
1912 Bechet, Paul E.
1921 Beck, Alfred Charles
1914 Beck, August Leo
1927 Beck, Davi

1911 Beekman, Fenwick
1905 Beer, Edwin
1906 Begg, Colin L.
1932 Beisler, Simon Anthony
1905 Beling, Christopher C.
1923 Bell, Alfred Lee Loomis
1904 Bell, George H.
1897 Bell, J. Finley
1925 Bell, Samuel Dennis
1918 Beller, Abraham J.
1930 Bendove, Raphael A.
1928 Benson, Reuel A.
1926 Benton, Nelson K.
1916 Berens, Conrad
1900 Berg, Albert A.
1927 Berg, Benjamin N.
1890 Berg, Henry W.
1923 Bergamini, Herbert M.
1928 Berkowitz, Bernard B.
1926 Berliner, Milton L.
1933 Berner, Frank
1928 Bernheim, Alice R.
1924 Bernstein, Max
1925 Berry, Frank B.
1900 Bickham, Warren S.
1901 Bierhoff, Frederic
1931 Bierman, William
1895 Biggs, George P.
1928 Biloon, Sol
1928 Binger, Carl A. L.
1928 Binkley, George E.
1927 Bishop, F. Warner
1893 Bishop, Louis F.
1932 Bishop, Louis F., Jr.
1930 Bishop, Philip George Crosbie
H.

1903 Bissell, Dougal
1915 Black, Florence A.
1910 Blackwell, Hugh B.
1932 Blakeslee, George A.
1910 Blank, Marcus I.
1932 Blanton, Smiley
1919 Blatteis, Simon R.
1896 Blodgett, Frank J.
1927 Bloom, David
1899 Bloom, Selina
1916 Blum, Theodor
1927 Blumenthal, J. Leon
1913 Blumgart, Leonard
1916 Blumgarten, Aaron S.
1921 Boas, Ernst P.
1918 Bodenheimer, Milton
1933 Bodo, Richard C.
1924 Boehm, Joseph L.
1926 Boenke, Rudolph
1926 Boese, William H.
1917 Boettiger, Carl
1925 Bohrer, John V.
1932 Bolduan, Charles Frederick
1916 Bonime, Ellis
1907 Bookman, Arthur
1918 Bookman, Milton R.
1920 Boorstein, Samuel W.
1885 Booth, J. Arthur
1927 Boots, Ralph H.
1916 Bortone, Frank
1933 Bosworth, David M.
1915 Bowers, Wesley C.
1932 Bowles, Ray McCune
1916 Boyd, Carlisle S.
1925 Boynton, Perry S.
1932 Bozsan, Eugene John
1907 Bradford, Stella S.
1931 Bradner, Renfrew
1914 Bradshaw, William M.
1931 Brandon, William R.
1929 Brandt, Murray Lampel
1908 Braun, Alfred
1930 Breidenbach, Lester
1917 Brennan, Robert E.
1930 Brennan, Thomas M.
1918 Brenner, Edward C.
1924 Brennglass, Joachim
1897 Brettauer, Joseph
1889 Brewer, George E.
1930 Brickner, Richard M.
1927 Bridges, Milton A.
1895 Brien, William M.
1930 Brighton, George Renfrew
1912 Brill, Abraham A.
1926 Broadwin, Isra T.
1927 Brock, Samuel
1904 Brodhead, George L.
1904 Brooks, Harlow
1922 Brown, Aaron
1912 Brown, Ethel Doty
1895 Brown, James Spencer
1901 Brown, Samuel A.
1932 Brown, Wade H.
1931 Bruce, Gordon M.
1918 Bruder, Joseph
1920 Brundage, Walter H.
1904 Bryant, William Sohier
1933 Buchman, Joseph
1929 Buckley, Robert
1910 Buckmaster, Clarence W.
1931 Buckstein, Jacob
1909 Buerger, Leo
1910 Bugbee, Henry G.
1927 Bull, David C.
1928 Bullard, Edward A.

1907 Bullowa, Jesse G. M.
1931 Bullwinkel, Henry G.
1927 Bunzel, E. Everett
1926 Burbank, Reginald
*1887 Burch, T. Hamilton
1930 Burchell, Samuel C.
1910 Burdick, Carl G.
1915 Burk, Samuel B.
*1886 Burke, Martin
1922 Burlingame, C. C.
1908 Burrows, Waters F.
1911 Busby, Archibald H.
1917 Butler, Eustace C.
1920 Butterfield, Paul M.
1928 Buvinger, Charles W.
1905 Byard, Dever S.
*1929 Byrd, Charles Wise
1914 Byrne, Joseph
1891 Cabot, John
1927 Caffey, John P.
1922 Cahill, George F.
1885 Caillé, Augustus
1918 Caldwell, William E.
1932 Calvelli, Eugene
1898 Camac, Charles N. B.
1928 Campbell, Meredith F.
1924 Cannon, A. Benson
1928 Carleton, Sprague
1921 Carlisle, John H.
1902 Carlisle, Robert J.
1921 Carlucci, Gaston A.
1922 Carp, Louis
1921 Carr, Frank C.
1886 Carr, Walter Lester
1928 Carrel, Alexis
1933 Carroll, John
1925 Carter, Rupert F.
1904 Carter, William W.
1931 Carty, John Russell
1920 Casamajor, Louis
1915 Cash, Stanmore L.
1931 Cashman, George A.
1906 Cassebeer, Henry A.
1905 Cassell, James W.
1910 Caturani, Michele G.
1921 Cave, Henry W.
1910 Cecil, Russell L.
1908 Chace, Arthur F.
1920 Chalmers, Thomas C.
1931 Chaney, L. Beverley
1886 Chapin, Henry D.
1920 Chaplin, Hugh
1904 Chard, Marie Louise
1914 Chargin, Louis
1924 Charlton, Herbert Richard
1922 Chase, Herbert C.
1932 Cheney, Clarence O.
1915 Cherry, Thomas H.
1896 Chetwood, Charles H.
1926 Chickering, Henry T.
1924 Chilian, Stephen A.
1932 Chobot, Robert
1933 Christensen, Bryant E.
1904 Clark, J. Bayard
*1896 Clark, L. Pierce
1922 Clark, Raymond
1879 Cleveland, Clement
1922 Cleveland, Mather
1911 Clock, Ralph O.
1894 Coakley, Cornelius G.
1931 Coburn, Alvin F.
1917 Coca, Arthur F.
*1892 Coffin, Lewis A.
1927 Cohen, Frances

*Deceased

1924 Cohen, Harry
1921 Cohen, Ira
1905 Cohen, Martin
1928 Cohen, Samuel A.
1910 Cohn, Alfred E.
1890 Cohn, Felix
1926 Cohn, Sidney
1910 Cole, Lewis Gregory
1909 Cole, Rufus I.
1915 Coleman, Joseph
1904 Coleman, Warren
1928 Coler, Eugene S.
1925 Coley, Bradley L.
1892 Coley, William B.
1910 Colie, Edward M., Jr.
1925 Collings, Clyde W.
1905 Collins, Charles F.
1898 Collins, Howard D.
1892 Collins, Joseph
1927 Colonna, Paul C.
1922 Colp, Ralph
1927 Combes, Frank C., Jr.
1900 Conner, Lewis A.
1927 Connery, Joseph E.
1905 Connors, John F.
1908 Cooke, Robert A.
1927 Cooney, John D.
1930 Cooper, Henry S. F.
1927 Cornell, Nelson W.
1927 Cornell, Van Alstyne
1923 Cornwall, Leon H.
1910 Corscaden, James A.
1898 Corwin, Theodore W.
1921 Coryell, Clarence C.
1929 Coryllos, Pol N.
1927 Cosgrave, Millicent M. A.
1928 Cosgrove, Samuel A.
1933 Co Tui, Frank
1926 Coughlan, James F.
1922 Courten, Henry C.
1925 Cowett, Max P.
1924 Cowles, Henry Clay
1931 Cracovaner, Arthur J.
1922 Craig, C. Burns
1927 Craig, Howard Reid
1932 Craig, John Dorsey
1924 Craig, Stuart L.
1908 Cramp, Walter C.
1921 Crampton, C. Ward
1926 Crane, Claude G.
1925 Craver, Lloyd F.
1910 Crigler, Lewis W.
1900 Crispin, Antonio M.
1912 Crohn, Burrill B.
1921 Cross, Frank B.
1926 Crump, Armistead C.
1922 Cudmore, John H.
1901 Culbert, William L.
1927 Cumbler, George W.
1921 Cunningham, W. F.
1915 Curtin, Thomas H.
1923 Cussler, Edward
1904 Cutler, Colman W.
1923 Cutler, Condict W., Jr.
1923 D'Albora, John B.
1931 D'Alton, Clarence J.
1886 Dana, Charles L.
1922 Dannreuther, Walter T.
1922 Danzer, Charles S.
1931 Danzis, Max
1928 Darlington, Charles G.
1904 Darlington, Thomas
1908 Darrach, William
1931 Davidoff, Leo M.
1932 Davidson, Harold B.
1926 Davidson, Leonard T.
1924 Davidson, Louis R.

1931 Davidson, Morris
1899 Davis, A. Edward
1909 Davis, George E.
1932 Davis, John Staige
1920 Davis, Thomas K.
1930 Davis, T. Wallis
1930 Davison, Charles
1933 Dawson, Martin H.
1922 Dean, Archie L., Jr.
1928 De Bellis, Hannibal
1933 Deery, Edwin M. G.
1904 de Forest, Henry P.
1927 De Graff, Arthur C.
1924 de Graffenried, Anthony F.
1928 de La Chapelle, Clarence E.
1929 Delatour, Beeckman J.
1880 Delavan, D. Bryson
1932 Delzell, William Robert
1890 Dench, Edward B.
1908 Denenholz, Aaron
1902 Denig, Rudolf
1932 Denison, Ward C.
1932 Denneen, Edward V.
1927 Dennen, Edward H.
1908 Dennett, Roger H.
1879 Dennis, Frederic S.
1916 Denno, Willard J.
1916 Denzer, Bernard S.
1931 Depping, Charles W.
1922 DeSanctis, Adolph George G.
1915 DeSanctis, Nicholas M.
1917 Detwiller, Albert K.
1932 deVictoria, Cassius L.
1926 Devlin, Joseph A.
1932 deVries, John K.
1921 deYoanna, Gaetano
1918 Diamond, Joseph S.
1891 Dickinson, Robert L.
1915 Dieffenbach, Richard H.
1890 Dillingham, Frederic H.
1924 Dineen, Paul A.
1922 di Palma, Salvatore
1906 Ditman, Norman E.
1906 Dixon, George S.
1929 Dochez, Alphonse Raymond
1922 Dodd, Raymond C.
1927 Doherty, Wm. Brown
1885 Dold, William E.
1921 Donaldson, Blake F.
1930 Donehue, Francis McG.
1924 Donnet, John V.
1928 Donovan, Daniel J.
1927 Donovan, Edward J.
1932 Dooley, Emmett A.
1920 Doran, William T.
1888 Dorning, John
1928 D'Oronzio, Joseph B.
1891 Doty, Alvah H.
1904 Dougherty, Daniel S.
1905 Douglas, John
1894 Douglass, H. Beaman
1923 Dourmashkin, Ralph L.
1900 Dow, Edmund LeRoy
1905 Downey, Martin
1911 Draper, George
1933 Druss, Joseph G.
1910 Du Bois, Eugene F.
1911 Du Bois, Francis E.
1919 Du Bois, Phebe Lott

1926 Du Bois, Robert O.
1917 Dudley, Guilford S.
1899 Duel, Arthur B.
1928 Duff, John
1927 Duffy, James J.
1893 Dunham, Theodore
1915 Dunning, Henry Sage
1916 Dunning, William M.
1921 Dunnington, John H.
1933 Duryee, Abram Wilbur
1923 Dwight, Kirby
1913 Dwyer, James G.
1927 Dwyer, William A.
1898 Eagleton, Wells P.
1927 Eastmond, Charles
1926 Easton, Charles D.
1927 Easton, E. R.
1922 Edelman, Leo
1922 Edelman, Moses H.
1903 Edgerton, F. Cruger
1933 Edlin, James S.
1921 Edwards, James B.
1921 Eggers, Carl
1915 Eggleston, Cary
1922 Eggston, Andrew A.
1931 Eglee, Edward P.
1927 Ehrenclou, Cora M.
1928 Eidson, Joseph P.
1891 Einhorn, Max
1924 Eisberg, Harry B.
1906 Eisenberg, Isidore C.
1904 Eising, Eugene H.
1933 Eiss, Stanley
1906 Eliot, Ellsworth, Jr.
1925 Eller, Joseph J.
1921 Elliott, Edward S.
1886 Elliott, George R.
1921 Elmendorf, Ten Eyck
1897 Elsberg, Charles A.
1928 Elser, William
1921 Elwyn, Herman
1894 Ely, Albert H.
1904 Emerson, Haven
1930 Emerson, Kendall
1902 Emerson, Linn
1911 Epstein, Albert A.
1908 Epstein, Sigmund
1910 Erdman, Seward
1892 Erdmann, John F.
1928 Evans, John N.
1897 Ewing, James
1905 Fahnestock, Ernest
1931 Falk, Emil A.
1916 Falk, Henry C.
1924 Famulener, Lemuel W.
1932 Fanoni, Vincenzo
1928 Farnum, Waldo B.
1909 Farr, Charles E.
1914 Farrar, Lilian K. P.
1910 Farrell, Benjamin P.
1910 Faulkner, E. Ross
1927 Faulkner, James F.
1904 Feinberg, Israel L.
1928 Feit, Hermann
1923 Felberbaum, David
1930 Felden, Botho F.
1922 Feldman, Samuel
1922 Felsen, Joseph
1907 Ferguson, Robert H.
1933 Ferraro, Armando
1891 Ferris, Albert W.
1931 Findley, Robert T.
1926 Fineman, Solomon
1922 Finke, George W.
1920 Finkelstein, Harry
1931 Finkle, Philip
1913 Finley, Caroline S.
1929 Fischer, Alfred Elias

1908 Fischer, Hermann
1890 Fischer, Louis
1928 Fish, George W.
1927 Fishberg, Arthur Maurice
1931 Fishberg, Ella H.
1913 Fishberg, Maurice
1886 Fisher, Edward D.
1918 Fisher, Judson C.
1930 Fisher, Robert C., 2nd
1924 Fiske, Edwin Rodney
1895 Fiske, James Porter
1916 Fitzgerald, Fred J. C.
1920 Fletcher, Norton DeL. L.
1905 Flexner, Simon
1922 Fobes, Joseph M.
1933 Foot, Nathan Chandler
1899 Foote, Edward M.
1914 Forbes, Henry Hall
1904 Ford, William M.
*1911 Foster, Nellis B.
1932 Fowler, Edmund Prince
1919 Fowler, Robert H.
1906 Fowler, Russell S.
1927 Fowlkes, John W.
1916 Fox, Elsie
1880 Fox, George H.
1904 Fox, Howard
1933 Francis, Charles C.
1932 Francis, Thomas, Jr.
1906 Frank, Robert T.
1913 Frankel, Edward, Jr.
1928 Frantz, Angus M.
1928 Frantz, Virginia K.
1920 Fraser, Alexander
1918 Fraser, John F.
1904 Frauenthal, Herman C.
1923 Freed, Frederick C.
1927 Freeland, Frank
1892 Freeman, Rowland G.
1931 Freston, Julian M.
1924 Freudenfall, Benjamin
1927 Freund, Meyer H.
1926 Frey, Walter G., Jr.
1886 Fridenberg, Albert H.
1933 Friedman, Benjamin
1918 Friedman, Emanuel D.
1932 Friedman, Jacob
1908 Friedman, Louis
1927 Fries, Margaret E.
1913 Friesner, Isidore
1907 Frink, Claude A.
1904 Frissell, Lewis F.
1919 Froehlich, Eugene
1930 Frosch, Herman L.
*1896 Frothingham, Richard
1912 Fuchsius, John H.
1921 Fulkerson, Lynn Lyle.
1931 Fuller, Clarence C.
1907 Furniss, Henry Dawson
1931 Gais, Elmer S.
1931 Galdston, Iago
1932 Galland, Walter I.
1900 Gant, Samuel G.
1916 Garbat, Abraham L.
1926 Garlock, John H.
1889 Garmany, Jasper J.
1921 Gatewood, William L.

*Deceased

1914 Gaudiani, Vincent
1931 Gavin, Helen
1926 Gay, Frederick P.
1916 Geiringer, David
1914 Geist, Samuel H.
1921 Gelber, Charles N.
1928 Gerber, Rubin A.
1910 Gerster, John C. A.
1929 Geyelin, H. Rawle
1901 Gibb, W. Travis
1930 Giblin, John
1893 Gibson, Charles L.
1894 Gilfillan, W. Whitehead
1906 Gillespie, David H. M.
1921 Gillette, Curtenius
1909 Gilmour, Andrew J.
1925 Ginsberg, George
1930 Ginsburg, Solomon
1931 Ginsburg, Sol W.
*1887 Girdner, John H.
1926 Gitlow, Samuel
1918 Glafke, William H.
1922 Glazebrook, Francis H.
1923 Globus, Joseph H.
1927 Glushak, Leopold I.
1918 Goeller, Charles J.
1928 Goetchius, Harry D.
1933 Goetsch, Arthur
1922 Goetsch, Emil
1927 Goff, Byron H.
1930 Gold, Harry
1900 Goldan, S. Ormond
1919 Goldberger, Isidore H.
1922 Goldberger, Lewis A.
1929 Goldberger, Morris Aaron
1927 Goldblatt, David
1931 Goldbloom, A. Allen
1923 Golden, Ross
1891 Goldenberg, Hermann
1928 Goldman, A. Milton
1928 Goldman, Charles
1933 Goldman, Irving Brice
1933 Goldmark, Carl
1928 Goldring, William
1930 Goldstein, Eli
1918 Goldstein, Isidore
1908 Goldwater, Sigismund S.
1930 Golub, Jacob Joshua
1922 Gonzales, Thomas A.
1922 Goodfellow, Lillian M.
1930 Goodfriend, Milton J.
1913 Goodfriend, Nathan
1906 Goodhart, S. Philip
1899 Goodman, Abraham L.
1903 Goodman, Charles
1931 Goodman, Henry I.
1924 Goodman, Herman
1906 Goodridge, Malcolm
1927 Gordon, Richard E.
1922 Gottesman, Julius
1922 Gottlieb, Charles
1922 Gottlieb, Mark J.
1915 Gould, Everett W.
1923 Grace, Roderick V.
1905 Grad, Hermann
1908 Graef, Charles
1925 Graham, John C.
1924 Graham, John R.
1933 Graham, Thomas Norris
1910 Grant, John P.

*Deceased

1889 Grauer, Frank
1909 Grausman, Philip M.
1919 Graves, Gaylord W.
1927 Gray, Irving
1904 Greeff, J. G. William
1905 Green, Nathan W.
1925 Greenberg, David
1928 Greenberger, Monroe E.
1933 Greene, Carl Hartley
1913 Greene, James S.
1926 Greene, Marius
*1891 Greene, Robert H.
1931 Greenhouse, Charles A.
1933 Greenwald, Harry M.
1927 Greenwald, Max
1932 Gregg, Alan
1908 Gregory, Menas S.
1932 Gresser, Edward Bellamy
1933 Grethmann, Wolfgang
1895 Griffin, Edwin H.
1931 Grinnell, Robert S.
1927 Gross, Louis
1915 Gross, Maurice H.
1909 Gross, Moritz
1928 Gross, Paul
1918 Grossman, Morris
*1928 Grout, Gerald H.
1918 Grushlaw, Israel
1914 Guile, Hubert V.
1909 Guion, Clarence C.
1927 Guion, Connie M.
1922 Gulliver, Francis D.
1929 Gutierrez, Robert
1898 Guttman, John
1909 Gwathmey, James T.
1901 Haas, Sidney V.
1909 Haberman, J. Victor
1927 Hahn, Leo J.
1927 Haiman, Julius Arky
1925 Hajek, Joseph
1904 Hale, Henry Ewing
1926 Hall, Fairfax
1933 Hall, Henry Lawrence
1918 Hall, John Mead
1933 Hallock, Leonard A.
1891 Hallock, Silas F.
1904 Halsey, Robert H.
1921 Halsted, Harbeck
1916 Hanford, John Munn
1933 Hanger, Franklin MacCue
1928 Hanley, James S.
1914 Hansen, Ejnar
1933 Hanssen, Eilif C.
1928 Hardy, Le Grand H.
1921 Harkavy, Joseph
1904 Harlow, Ellwood
1930 Harrington, Helen
1931 Harris, Augustus
1929 Harris, John Huggins
1921 Harris, Louis I.
1894 Harris, Thomas J.
1933 Harris, William
1904 Hart, T. Stuart
1911 Hartshorn, Winfred M.
1917 Hartshorne, Isaac
1932 Hartung, Edward F.
1912 Hartwell, Henry A.
1901 Hartwell, John A.
1931 Harvey, Harold D.
1897 Harvey, Thomas W.
1918 Hasbrouck, James F.

*Deceased

1925 Haseltine, Sherwin L.
1902 Haskin, William H.
1922 Hatcher, Robert A.
1928 Hauser, Edwin T.
1927 Hausman, Louis
1923 Hauswirth, Louis
1895 Hawkes, Forbes
1922 Hawkins, William H.
1921 Hawks, Everett M.
1932 Hayes, James Joseph
1901 Hayes, William Van V.
1907 Haynes, Royal S.
1909 Hays, Harold M.
1926 Healey, William V.
1918 Healy, William P.
1933 Heaton, Claude Edwin
1895 Heiman, Henry
1918 Heine, Joseph
1890 Heitzmann, Louis
1918 Held, Isidore W.
1910 Heller, Isaac M.
1932 Heller, Nathan B.
1909 Hellman, Alfred M.
1926 Henline, Roy Biggs
1933 Hennell, Herman
1921 Hennessy, James P.
1908 Hensel, Otto
1927 Herendeen, Ralph E.
1928 Herman, Harold
1910 Herrick, William W.
1922 Herriman, Frank R.
1902 Herrman, Charles
1919 Hertz, Julius J.
1911 Herzig, Arthur J.
*1906 Hess, Alfred F.
1922 Hetrick, Llewellyn E.
1933 Heuer, George J.
1914 Heyd, Charles Gordon
1931 Heyl, James Harry
1932 Hicks, Hugh M.
1922 Higgins, William M.
1910 Highman, Walter J.
1933 Higinbotham, Norman L.
1903 Hill, Ira L.
1914 Hillman, Oliver S.
1909 Hinkle, Beatrice M.
1927 Hinsie, Leland E.
1925 Hinton, J. William
1913 Hirsch, I. Seth
1921 Hirsh, A. Bern
1931 Hirst, Virginius B.
1904 Hitzrot, James M.
1921 Hoch, George F.
1928 Hoenig, Edward
1911 Hoguet, Joseph P.
1909 Holden, Frederick C.
1894 Holden, Ward A.
1920 Holladay, Edwin W.
1907 Holland, Arthur L.
1925 Hollander, Edward
1930 Holt, Evelyn
1930 Homrich, Leslie A.
1921 Honan, William F.
1887 Honegger, Oscar P.
1924 Hooker, Henry L.
1906 Hooker, Ransom S.
1904 Hopkins, Frank T.
1926 Hopkins, J. Gardner
1928 Horn, Herman
1901 Horn, John
1922 Horn, Walter L.
1913 Horowitz, Philip
1928 Hory, Joseph S.

*Deceased

1923 Hough, Perry B.
1913 Houghton, Harris A.
1930 Howard, Frederick H.
1925 Howard, Robert C.
1923 Howe, Alexander C.
1919 Howe, Hubert S.
1931 Howell, John Taylor, Jr.
1926 Hoyt, Harold E.
1896 Hubbard, William N.
1901 Hubby, Lester M.
1885 Huber, Francis
1911 Huber, Frederick W.
1923 Hubert, Louis
1919 Huddleson, James H.
1919 Huey, Arthur J.
1928 Hughes, Wendell L.
1910 Huhner, Max
1928 Hume, Edward H.
1927 Humphreys, Frederick B.
1916 Humphries, Robert E.
1924 Hunt, Charles Jack
1905 Hunt, Edward L.
1903 Hunt, J. Ramsay
1917 Hunt, Westley M.
1925 Huppert, Elmer I.
1901 Hurd, Lee M.
1924 Hurd, Ralph A.
1933 Hurley, Vincent
1920 Hutchinson, Abbott T.
1928 Hutchinson, Robert H., Jr.
1928 Hutton, Robert L.
1912 Huvelle, Rene H.
1918 Hyams, Joseph A.
1928 Hyams, Mortimer N.
1882 Hyde, Frederick E.
1910 Hyman, Abraham
1924 Hyman, Harold T.
1903 Hymanson, Abraham
1927 Hyslop, George H.
1894 Ill, Edward J.
1923 Imboden, Harry M.
1910 Imperatori, Charles J.
1918 Ingerman, Sergius M.
1908 Ippolito, Gennaro
1924 Irish, William H.
1922 Irving, George R.
1913 Irving, Peter
1909 Isaacs, Harry E.
1915 Ives, Robert F.
1929 Ivimey, Muriel
1908 Jaches, Leopold
1928 Jacobi, Harry G.
1932 Jacobi, Mendel
1926 Jacobsohn, Victor J.
1927 Jacoby, Adolph
1885 Jacoby, George W.
1904 Jacoby, J. Ralph
1904 Jaeger, Charles H.
1933 Jaffe, Henry Lewis
1910 Jaffin, Abraham E.
1916 James, Henry
1928 James, Wm. L.
1930 Janes, Martin Lewis
1913 Jarcho, Julius
1900 Jarecky, Herman
*1905 Jarvis, Nathan S.
1930 Jasper, M. Newton
1919 Jeck, Howard S.
1900 Jelliffe, Smith Ely
1914 Jellinghaus, C. Frederic

*Deceased

1921 Jennings, John E.
1932 Jerskey, Abraham
1926 Jessup, David S. D.
1922 Jessup, Everett C.
1922 Joachim, Henry
1927 Jobling, James W.
1918 Johnson, F. Elmer
1910 Johnson, Frederic M., Jr.
1930 Johnson, Scott
1924 Johnson, Thomas H.
1933 Johnson, Vansel S.
1918 Jones, David H.
1922 Jones, Marvin F.
1930 Jones, Oswald R.
1921 Joseph, Morris
1927 Joughin, James L.
1927 Joyner, James C.
1904 Judd, Aspinwall
1922 Judd, Harold B.
1931 Jungeblut, Claus W.
1933 Kahle, Ralph Charles
1927 Kahn, Isador W.
*1912 Kahn, L. Miller
1918 Kahn, Morris H.
1909 Kaliski, David J.
1917 Kantor, John L.
1926 Kaplan, Ira I.
1927 Kardiner, Abraham
1930 Karelitz, Samuel
1910 Kast, Ludwig
1922 Kaufman, Louis R.
1906 Kaufmann, Jacob
1928 Keating, John J. H.
1932 Keil, Frank Conrad
1909 Keller, Frederick C.
1927 Keller, Henry
1922 Kelley, Catherine Rose
1933 Kelley, Eugene F.
1909 Kellogg, Edward L.
1929 Kellogg, William A.
1912 Kennedy, Foster
1926 Kennedy, Robert H.
1927 Kennedy, William T.
1927 Kenworthy, Marion E.
1904 Kenyon, James H.
1924 Kenyon, Josephine H.
1905 Keppler, Carl R.
1933 Keresztúri, Camille
1899 Kerley, Charles G.
1919 Kerley, James H.
1932 Kern, E. Clarence
1913 Kernan, John D., Jr.
1901 Kerrison, Philip D.
1922 Keschner, Moses
1931 Kesten, Beatrice M.
1931 Kesten, Homer D.
1915 Key, Ben Witt
1898 Keyes, Edward L.
1919 Keyes, Harold B.
1912 Kilbane, Edward F.
1933 Kilroe, John Charles
1931 Kimball, Francis N.
1920 Kindred, John J.
1915 King, James J.
1920 King, Joseph E. J.
1930 King, S. Edward
1906 Kingsbury, Jerome
1926 Kirby, Daniel Bartholomew
1918 Kirby, George H.
1922 Kirwin, Thomas J.
1923 Klaus, Henry

*Deceased

1932 Kleegman, Sophia J.
1922 Klein, William
1914 Kleinberg, Samuel
1930 Kleinfeld, Louis
1928 Klemperer, Paul
1930 Klenke, Dorothy A.
1923 Klepper, Julius I.
1926 Klingenstein, Percy
1933 Klingman, Walter O.
1927 Klotz, Walter C.
1897 Knapp, Arnold H.
1922 Knapp, Richard E.
1931 Knauth, Marjorie L.
1918 Knight, Frank H.
1907 Knipe, William H. W.
1897 Knopf, S. Adolphus
1921 Knopf, Saul
1926 Knox, Leila Charlton
1927 Koenig, George A.
1931 Koffler, Arnold
1922 Koffler, Emil
1924 Kohn, Jerome L.
1927 Kohn, Louis Winfield
1898 Koller, Carl
1906 Kopetzky, Samuel J.
1904 Kosmak, George W.
1911 Kovacs, Richard
1927 Kraetzer, Arthur F.
1927 Kramer, Benjamin
1927 Kramer, Rudolph
1920 Kraus, Walter M.
1930 Krech, Shepard
1923 Krida, Arthur
1922 Kross, Isidor
1917 Krug, Ernest F.
1933 Kruna, Richard B.
1926 Kruskal, Isaac David
1932 Kubie, Lawrence S.
1928 Kuhlman, Alvin E.
1927 Kurzrock, Julius
1928 Kurzrok, Raphael
1930 Kurzweil, Peritz M.
1930 Kutisker, Meyer J.
1926 Ladd, William Sargent
1891 Ladin, Louis J.
1898 LaFetra, Linnaeus E.
1921 Laidlaw, George F.
1904 Laighton, Florence M.
1931 Lally, Jordan
1912 Lamb, Albert R.
1910 Lambert, Adrian V. S.
1893 Lambert, Alexander
1907 Lambert, Frederick E.
1930 Lambert, Robert K.
1891 Lambert, Samuel W.
1930 Landon, John F.
1918 Landsman, Arthur A.
1932 Landsteiner, Karl
1921 Lange, Louis C.
1922 Langmann, Alfred G.
1918 Langrock, Edwin G.
1910 Laporte, George L.
1897 Lapowski, Boleslaw
1931 La Rotonda, Oswald
1922 Lasher, Willis W.
1922 Lattin, Berton
1930 Lavalle, Peter
1920 Lavandera, Miguel
1920 Lavell, Thomas E.
1926 La Vigne, Alexander A.
1917 Lavinder, Claude H.
1908 Law, Frederick M.
1927 Laws, Carl Henry
1926 Lazarus, Joseph Arthur
1932 Leader, Sidney D.

1921 Leahy, Sylvester R.
1908 Leale, Medwin
1921 Lederer, Max
1897 Lederman, Moses D.
*1904 Lee, Burton J.
1928 Lee, George Bolling
1930 Leff, Morris
1928 Lehrman, Philip R.
1931 Lenz, Maurice
1914 Leo, Johanna B.
1910 Leopold, Jerome S.
1924 L'Episcopo, Joseph B.
1928 Lerner, Charles
1916 L'Esperance, Elise S.
1926 Lester, Charles Willard
1932 Levene, Phoebus A.
1905 Levin, Isaac
1919 Levin, Oscar L.
1931 Levine, Joseph
1929 Levine, Morris
1927 Levine, Samuel Z.
1933 Levy, David M.
1927 Levy, Ralph J.
1922 Levy, Robert L.
1911 Le Wald, Leon T.
1906 Lewi, Emily
1932 Lewi, Maurice J.
1932 Lewis, George M.
1932 Lewis, Jacques M.
1927 Lewis, Kenneth M.
1922 Lewis, Raymond W.
1897 Lewis, Robert
1908 Lewisohn, Richard
1918 Lewy, Raphael
1900 Libman, Emanuel
1910 Lieb, Charles C.
1920 Lieb, Clarence W.
1924 Lightstone, Abraham
1927 Likely, David Stanley
1933 Lilien, Adolph A.
1891 Lilienthal, Howard
1927 Lincoln, Asa Liggett
1927 Lincoln, Edith M.
1929 Lincoln, James R.
1918 Lindeman, Howard E.
1917 Linder, William
1926 Lintz, Joseph
1930 Lippmann, Robert K.
1927 Lipsett, Philip J.
1932 Lipsky, Merrill D.
1933 Lisa, James R.
1908 Littell, Elton G.
1924 Littwin, Charles
1933 Livingston, Edward M.
1910 Lloyd, Henry W.
1927 Lloyd, Ralph I.
1927 Loeb, Martin J.
1929 Loeb, Robert F.
1930 Loebel, Robert O.
1931 Logie, H. Burton
1927 Lohman, William H.
1931 Loizeaux, Leon S.
1920 Lombardo, Melchiore
1906 Long, Eli
1914 Long, William B.
1919 Lopez, Jose Antonio
1926 Loré, John Marion
1933 Loth, Mathilde
1928 Lough, Walter G.
1905 Loughran, Robert L.
1933 Lowenfish, F. Philip
1931 Lowrey, Lawson G.
1916 Lowsley, Oswald S.
1932 Lubash, Samuel

*Deceased

1922 Lucus, Thomas D'Arcy
1927 Ludlow, George C.
1924 Luippold, Eugene John
1927 Luke, H. Clifton
1898 Lusk, William C.
1927 Lutz, J. Raymond
1905 Lyle, Henry H. M.
1908 Lyle, William G.
1929 Lynch, Jerome M.
1898 Lynch, John B.
1926 Lyon, Edward C., Jr.
1930 Lyons, Hubert A.
1933 Lyons, L. Vosburgh
1930 Lyons, Morris A.
1922 Lyttle, John D.
1895 McAlpin, David H.
1916 McAlpin, Kenneth R.
1901 McAuliffe, George B.
1928 McAuliffe, Gervais W.
1903 McBarron, John D.
1918 McCabe, John
1909 McCarthy, Joseph F.
1912 McCastline, William H.
1933 McConnell, Robert Hall
1899 McCoy, John Charles
*1904 McCoy, John J.
1905 McCreery, Forbes R.
1914 McCreery, John A.
1904 McCullagh, Samuel
1929 McDaniel, Floyd C.
1921 McDannald, Clyde E.
1902 McDonald, Dennis J.
1930 McDonald, Richard Joseph
1927 MacFee, William F.
1927 McGowan, Frank J., Jr.
1922 McGrath, John F.
1903 McGrath, John J.
1928 McGraw, Robert B.
1931 MacGregor, J. Arnot
1929 McGuinness, Madge C. L.
1919 MacGuire, Constantine J., Jr.
1922 MacGuire, Daniel P.
1897 MacHale, Ferdinand S.
1920 McHenry, Junius H.
1925 McIntosh, Rustin
1908 MacKee, George M.
1921 McKendree, Charles A.
1920 McKenna, William F.
1932 Mackenzie, Locke
1927 MacKenzie, Luther B.
1932 McKeown, Hugh S.
1894 McKernon, James F.
1927 McKinney, John McDowell
1931 McLave, Evan W.
1928 MacLean, Aubrey B.
1930 McLean, William
1911 MacLeod, William P.
1932 McMaster, Philip D.
1920 MacNeal, Ward J.
1917 McNeill, Walter H., Jr.
1905 MacPhee, John J.

*Deceased

1908 Macpherson, Duncan
1909 McPherson, Ross
1928 McQuillan, Arthur S.
1924 MacRobert, Russell G.
1920 McSweeny, Edward S.
1894 Mabbott, J. Milton
1930 Mackie, Thomas Turlay
1928 Mage, Sigmund
1923 Magid, Maurice O.
1927 Magida, Nathan
1913 Malcolm, Percy E. D.
1930 Malloch, Archibald
1920 Maloney, Edward R.
1914 Mandel, Arthur R.
1928 Mandelbaum, M. Joseph
1892 Manges, Morris
1925 Manheim, Sigmund
1917 Manley, Herbert D.
1923 Mann, Hubert
1897 Mann, John
1927 Mann, Lewis T.
1904 Mannheimer, George
1913 Manning, G. Randolph
1933 Marcus, Joseph M.
1921 Marine, David
1933 Marino, A. W. Martin
1932 Marmorston-Gottesman, Jessie
1913 Marsh, Elias J.
1928 Martin, Alexander T.
1928 Martin, Kirby A.
1911 Martin, Thomas A.
1906 Martin, Walton
1930 Martland, Harrison S.
1927 Marton, Louis
1909 Mason, Howard H.
1927 Master, Arthur M.
1931 Masterson, John J.
1904 Mathews, Francis S.
1927 Matsner, Eric M.
1909 Matthews, Frank C.
1924 Matthews, Frederick J.
1928 Matthews, Harvey B.
1886 May, Charles H.
1907 May, William Ropes
1918 Maybaum, Jacob L.
1918 Mayer, Leo
1933 Mayer, Max David
1932 Maynard, Edwin Post, Jr.
1929 Meek, Raymond E.
1916 Meeker, Harold D.
1932 Meeker, Louise H.
1922 Meichner, Frederick H., Jr.
1900 Meierhof, Edward L.
1927 Meleney, Frank L.
1932 Mencher, William H.
1918 Mencken, Harry P.
1931 Merrill, E. Forrest
1924 Merritt, Katherine K.
1902 Mersereau, William J.
1930 Merwarth, Harold Russell
1929 Mettenleiter, Michael W.
1885 Meyer, Alfred
1925 Meyer, Herbert W.
1930 Meyer, Monroe A.
1931 Meyer, William Henry
1921 Meynen, George K.
1907 Michaelis, Alfred
1904 Michailovsky, M.

1912 Michel, Leo L.
1918 Milbank, Samuel
1927 Milch, Henry
1933 Milici, Attilio
1933 Miller, Charles S.
1904 Miller, George N.
1920 Miller, Heymen R.
1904 Miller, James Alexander
1933 Miller, Julius A.
1931 Miller, Laura
1931 Millet, John A. P.
1906 Milliken, Seth M.
1901 Mills, Jackson M.
1924 Mills, Nathaniel
1919 Miner, Donald
1932 Minsky, Henry
1917 Mitchell, Charles R.
1925 Mitchell, Wendell
1910 Mittendorf, Alfred D.
1916 Mixsell, Harold R.
1926 Moench, Gerard L.
1922 Moffat, Barclay W.
1913 Moffett, Rudolph D.
1889 Monaelesser, Adolph
1928 Montgomery, Andrew H.
1933 Moon-Adams. Dabney
1904 Mooney, Henry W.
1909 Moore, Albertus A.
1904 Moorhead, John J.
1931 Moretsky, Henry M.
1927 Morhard, Francis L.
1922 Morrill, Ashley B.
1923 Morris, John H.
1890 Morris, Lewis R.
1891 Morris, Robert T.
1927 Morrison, William W.
1925 Morrissey, John H.
1916 Morrow, Albert S.
1930 Morse, Joseph L.
*1891 Mortimer, W. Golden
1930 Morton, Dudley J.
1897 Morton, Henry H.
1929 Morton, Paul Colhoun
*1900 Moschcowitz, Alexis V.
1906 Moschcowitz, Eli
1907 Mosenthal, Herman O.
1924 Moss, Abraham
1908 Moss, L. Howard
1913 Mount, Walter B.
1933 Moyle, Eugene Henry
1932 Muehleck, George E.
1909 Mulholland, Joseph A.
1927 Murphy, James B.
1922 Murray, Clay Ray
1929 Murray, Foster
1924 Myers, Florizel deL.
1905 Myers, Howard G.
1925 Myers, Lotta Wright
1926 Myerson, Mervin C.
1889 Myles, Robert C.
1928 Nardiello, Vincent A.
1929 Nash, Edward M.
1903 Nathan, Philip W.
1921 Neal, Josephine B.
1923 Neer, Edmonde De Witt
1902 Neer, William
1902 Neergaard, Arthur E.
1928 Neff, Lewis K.
1927 Neilson, John, Jr.
1931 Neivert, Harry

*Deceased

1928 Nelson, Ray S.
1932 Nemet, Geza
1909 Neuhof, Harold
1918 Neustaedter, Marcus
1933 Neustaedter, Theodore
1930 Newman, David A.
1922 Ney, K. Winfield
1931 Nicholls, Edith E.
1933 Niles, Henry D.
1908 Niles, Walter L.
1918 Nilsen, Arthur
1917 Nilson, S. John
*1905 Norrie, Van Horne
1906 Norris, Charles
1928 Northcott, Thomas A.
1932 Northington, Page
1886 Northrup, William P.
1906 Norton, Nathaniel R.
1897 Noyes, William B.
1908 Nutt, John J.
1912 Oastler, Frank R.
1918 Oberndorf, Clarence P.
1931 Oberrender, Girard F.
*1910 Ochs, Benjamin F.
1930 O'Connor, Francis W.
1930 O'Connor, H. A. D.
1885 Offenbach, Robert
1904 Ogilvy, Charles
1932 Olitsky, Peter K.
1933 Opie, Eugene Lindsay
1906 Oppenheimer, Bernard S.
1912 Oppenheimer, Edgar D.
1910 Orgel, David H.
1927 Orgel, Samuel Z.
1927 Ornstein, George G.
1928 Orton, Henry B.
1932 Orton, Samuel Torrey
1904 Osgood, Alfred T.
1908 Osgood, Charles
1911 Ottenberg, Reuben
1927 Otto, Harold L.
1908 Oulmann, Ludwig
1928 Owre, Alfred
1933 Pack, George Thomas
1909 Packard, Maurice
1906 Page, John R.
1931 Paige, Beryl Holmes
1921 Palefski, Israel O.
1921 Palmer, Arthur
1922 Palmer, Walter W.
1915 Pappenheimer, Alwin M.
1923 Pardee, Harold E. B.
1923 Pardee, Irving H.
1892 Park, William H.
1906 Parker, Ransom J.
1906 Parodi, Teofilo
1908 Parounagian, Mihran B.
1931 Parsons, C. J. F.
1922 Parsons, William Barclay, Jr.
1911 Pascal, Henry S.
1904 Patterson, Henry S.
1932 Patterson, Howard A.
1927 Patterson, Russel H.
1930 Pattison, Jean Harwood
1933 Pearce, Louise
1926 Pearlstein, Frank
1913 Pease, Marshall C., Jr.
1931 Peck, Samuel M.

*Deceased

*1886 Peckham-Murray, Grace
1898 Pedersen, James
1904 Pedersen, Victor C.
1895 Peet, Edward W.
1923 Peightal, Thomas C.
1926 Pennoyer, Grant P.
1928 Perilli, Charles A.
1928 Perkins, Orman C.
1929 Perkins, Osborn P.
1930 Perla, David
1929 Perlberg, Harry J.
1917 Perrone, Ettore
1931 Peters, Frank H.
1905 Peterson, Edward W.
1888 Peterson, Frederick
1922 Philips, Herman B.
1886 Phillips, Wendell C.
1922 Phillips, W. Gray
1922 Pickhardt, Otto C.
1928 Pierce, Lee R.
1923 Pierson, Richard N.
1926 Platt, Anna
1928 Plaut, Alfred
1911 Plummer, Harry E.
1920 Poll, Daniel
1924 Pollak, Alfred W.
1891 Pollitzer, Sigmund
1933 Poltchaninoff, Nicholas J.
1928 Pomeranz, Maurice M.
1919 Pond, Erasmus A.
1904 Pool, Eugene H.
1931 Pope, Edgar M.
*1891 Porter, William H.
1931 Potter, Howard W.
1924 Potter, Philip C.
1913 Pou, Robert E.
1931 Pound, Robert E.
1931 Pratt, George K.
1927 Previtali, Giuseppe
1931 Prewitt, Proviso V.
1927 Prime, Frederick
1907 Proctor, James W.
1905 Prout, Thomas P.
1933 Pudney, William Kent
1894 Pulley, William J.
1915 Pumyea, P. Clinton
1902 Putnam, Charles R. L.
1932 Pyle, Louis Apgar
1920 Pyle, Wallace
1921 Quick, Douglas A.
1911 Quimby, A. Judson
1891 Quintard, Edward
1933 Rabiner, Abraham Max
1921 Rabinowitz, Meyer A.
1922 Rafsky, Henry A.
1927 Rahte, Walter E.
1929 Raisbeck, Milton J.
1931 Ralli, Elaine P.
1918 Ramirez, Maximilian A.
1916 Ramsdell, Edwin G.
1924 Randall, John A.
1925 Randel, William A.
1909 Randolph, John M.
1926 Ransohoff, Nicholas S.
1932 Rappleye, Willard C.
1927 Rashbaum, Maurice
1920 Rathbun, Nathaniel P.
1925 Ratner, Bret
1918 Ratnoff, Hyman L.

*Deceased

1931 Ratnoff, Nathan O.
1914 Rawls, Reginald McC.
1926 Read, J. Sturdivant
1901 Rector, Joseph M.
1928 Reed, Elias A.
1928 Reese, Algernon B.
1914 Rehling, Martin
1931 Reich, Arthur M.
1930 Reich, Carl
1921 Reid, John J., Jr.
1924 Reiss, Joseph
1914 Remer, John
1927 Restin, Erich H.
1912 Reuben, Mark S.
1925 Reynolds, Frederick P.
1930 Reynolds, Margaret R.
1927 Reznikoff, Paul
1932 Rhoads, Cornelius P.
1926 Rhodebeck, Edmund J.
1887 Rice, Clarence C.
1921 Rice, Frederick W.
1904 Richards, John D.
1910 Richards, John H.
1928 Richter, Maurice N.
1908 Riesenfeld, Edwin A.
1909 Rieser, Willy
1932 Riley, Edward J.
1919 Riley, Henry Alsop
1919 Rimer, Edward S.
1917 Ringer, Adolph I.
1932 Ringer, Michael
1932 Riordan, Timothy J.
1922 Ritter, Henry H.
1925 Ritter, J. Sidney
1926 Ritter, Saul A.
1931 Rivers, Thomas M.
1924 Robbin, Lewis
1907 Robbins, Felicia A.
1919 Roberts, Dudley De V.
1928 Roberts, Kingsley
1910 Roberts, Percy W.
1923 Robertson, Victor A.
1923 Robins, Bernard L.
1927 Robinson, G. Allen
1929 Robinson, G. Canby
1912 Robinson, John A.
1928 Robinson, Lewis B.
1910 Robinson, Meyer R.
1910 Robinson, William J.
1927 Rodgers, Mortimer William
1920 Roemer, Jacob
1927 Rogatz, Julian L.
1905 Rogers, John
1919 Rohde, Max S.
1927 Rohdenburg, G. L.
1915 Rongy, Abraham J.
1908 Roper, Joseph C.
1928 Rose, Ben-Henry
1916 Rosen, Isadore
1928 Rosen, Samuel
1911 Rosenbluth, Benjamin
1922 Rosenblüth, Milton B.
1927 Rosenfeld, Samuel S.
1923 Rosenheck, Charles
1922 Rosensohn, Meyer
1928 Rosenson, William
1906 Rosenthal, Max
1933 Rosenthal, Theodore
1922 Rosett, Joshua
1928 Ross, John
*1918 Rost, William L.
1919 Rostenberg, Adolph

*Deceased

1906 Roth, Henry
1932 Roth, Irving R.
1922 Rothschild, Marcus A.
1930 Rous, Peyton
1912 Rowland, Harry H.
1923 Rubin, Isidor C.
1921 Rulison, Ray H.
1931 Russell, Frederick F.
1908 Russell, James I.
1922 Russell, Thomas Hendrick
1933 Ryan, Charles Diller
1909 Ryder, George H.
1930 Sabin, Florence R.
1887 Sachs, Bernard
1930 Sackett, Nelson B.
1927 Sagal, Zachary
1933 St. George, Armin
1915 St. John, Fordyce B.
1920 St. Lawrence, William P.
1918 Salisbury, Lucius A.
1925 Salzer, Benjamin
1918 Sammis, Jesse F.
1913 Samuels, Bernard
1927 Samuels, Saul S.
1923 Sanders, Theodore M.
1921 Sands, Irving J.
1933 Sanman, Louis F.
1918 Satenstein, David L.
1927 Satterlee, Henry S.
1882 Satterthwaite, Thomas E.
1930 Saunders, Edward W.
1927 Saunders, Harry Clayton
1919 Saunders, Truman L.
1920 Sautter, Carl Marion
1915 Savini, Carlo
1933 Savitsky, Nathan
1926 Sawhill, John E.
1932 Sawyer, Wilbur A.
1927 Saxl, Newton T.
1918 Scadron, Samuel J.
1918 Scal, J. Coleman
1933 Scarff, John Edwin
1911 Schapira, Samuel W.
1927 Scheer, Henry M.
1917 Scheer, Max
1927 Schick, Bela
1931 Schilder, Paul F.
1923 Schiller, Abraham N.
1903 Schley, Winfield S.
1908 Schlichter, Charles H.
1918 Schlivek, Kaufman
1911 Schloss, Oscar M.
1932 Schmidt, Otto V. M.
1908 Schnepel, George A.
1912 Schoenberg, Mark J.
1930 Schreiber, Martin
1918 Schroeder, Louis C.
1930 Schroeder, William, Jr.
1928 Schullinger, Rudolph N.
1920 Schulman, Maximilian
1912 Schultze, Ernest C.
1927 Schwartz, C. Wadsworth
1915 Schwartz, Hans J.
1928 Schwartz, Irving
1929 Schwartz, Joseph
1928 Schwartz, Sidney P.
1906 Schwarz, Herman
1917 Schwerdtfeger, Otto M.
1922 Scott, Augusta
1907 Scott, George Dow
1925 Scott, James R.
1925 Seecof, David P.

1933 Selby, Nathaniel E.
1932 Selig, Seth
1922 Selinger, Jerome
1931 Selinsky, Herman
1904 Semken, George H.
1931 Senger, Fedor L.
1911 Senior, Harold D.
1931 Severance, Robert
1932 Seward, Jackson A.
1924 Seymour, Nan Gilbert
1921 Shailer, Sumner
1926 Shann, Herman
1921 Shapiro, Louis G.
1926 Shapiro, Louis L.
1929 Shapiro, Matthew
1926 Sharlit, Herman
1902 Sharp, J. Clarence
1914 Sharpe, William
1920 Shattuck, Howard F.
1905 Shearer, Leander H.
1918 Sheehan, J. Eastman
1907 Sheffield, Herman B.
1905 Shelby, Edmund P.
1931 Sheldon, Paul B.
1929 Shelley, Harold John
1932 Sheplar, Adele E.
1909 Sherman, Elbert S.
1920 Sherwin, Carl Paxson
1910 Shine, Francis W.
1918 Shlenker, Milton A.
1933 Shoenfeld, Dudley D.
1931 Shore, Benjamin R.
1928 Shwartzman, Gregory
1928 Silbert, Samuel
1932 Silver, Henry
·1880 Silver, Henry Mann
1893 Silver, Lewis Mann
1928 Simons, Irving
1933 Sims, Charles Franklyn
1921 Siris, Irwin E.
1912 Sittenfield, Maurice J.
1933 Skeel, Henry Robertson
1921 Skinner, Clarence E.
1922 Slattery, George N.
1932 Sloan, Lawrence Wells
1932 Slocum, C. Jonathan
1932 Smetana, Hans
1923 Smith, Alan DeForest
1928 Smith, Beverly C.
1917 Smith, Charles A.
1914 Smith, Charles Hendee
1916 Smith, Clarence H.
1930 Smith, Frank R.
1901 Smith, Harmon
1918 Smith, J. Morrissett
1924 Smith, James W.
1930 Smith, Lawrence Weld
1919 Smith, Martin DeF.
1927 Smith, Morley T.
1916 Smith, Morris K.
1923 Sneed, William L.
1918 Snow, William F.
1923 Snyder, Orlow C.
1913 Snyder, R. Garfield
1933 Sobel, Irwin P.
1904 Solley, Fred P.
1927 Solley, Frederick W.
1905 Solley, John B., Jr.
1933 Solley, Robert Folger
1928 Solomon, Harry A.
1893 Sondern, Frederic E.
1925 Sonnenschein, Harry D.
1910 Soresi, Angelo L.
1902 Sour, Bernard

1894 Southworth, Thomas S.
1922 Sovak, Francis W.
1927 Spain, Will Cook
1921 Spaulding, Edith Rogers
1917 Spaulding, Harry Van N.
1928 Speiser, Mortimer D.
1918 Spencer, Henry J.
1910 Spickers, William
1920 Spiegel, Leo
1923 Spielberg, William
1922 Spies, Edward A.
1927 Spillman, Ramsay
1901 Squier, J. Bentley
1931 Stainsby, Wendell J.
1932 Stanley-Brown, Margaret
1922 Stark, Jesse B.
1889 Stearns, Henry S.
1880 Stedman, Thomas L.
1904 Steese, Edwin S.
1922 Steffen, Walter C. A.
1908 Stein, Arthur
1932 Stein, Herbert Edward
1909 Stein, Sydney A.
1918 Steinach, William
1928 Steinbugler, Wm. F. C.
1925 Steiner, Joseph M.
1928 Stenson, Walter T.
1924 Stephens, Richmond
1925 Stepita, C. Travers
1905 Stern, Abram Richard
1917 Stern, Adolph
1908 Stern, Arthur
1928 Stetson, Dudley D.
1919 Stetson, Rufus E.
1907 Stetten, De Witt
1909 Stevens, Alex. Raymond
1919 Stevens, Charles W.
1916 Stevenson, George
1922 Stevenson, Holland N.
1927 Stevenson, Lewis
*1895 Stewart, George David
1930 Stewart, Harold J.
1918 Stewart, John D.
1912 Stewart, William H.
1911 Stillman, Alfred, 2d.
1923 Stillman, Edgar
1918 Stillman, Ernest G.
1911 Stillman, Ralph G.
1931 Stimson, Barbara B.
1921 Stimson, Philip M.
1922 Stivelman, Barnet P.
1913 Stockard, Charles R.
1933 Stoloff, E. Gordon
1927 Stone, William Ridgely
1898 Stone, William S.
1930 Stoner, William H.
1920 Stookey, Byron P.
1924 Stout, Arthur Purdy
1919 Stowell, David D.
1918 Strachstein, Abraham
1904 Strang, Walter W.
1908 Strauss, Israel
1930 Strauss, Spencer Goldsmith
1928 Strodl, George T.
1917 Strong, Samuel M.
1887 Stubenbord, William

*Deceased

1930 Studdiford, William E., Jr.
1908 Sturges, Leigh F.
1901 Sturmdorf, Arnold
1927 Sturtevant, James M.
1919 Sturtevant, Mills
1912 Sullivan, Raymond P.
1931 Sulzberger, Marion B.
1933 Summerill, Frederick
1909 Sutherland, Fred B.
1927 Sutton, John E., Jr.
1927 Sutton, Lucy Porter
1927 Sweet, Joshua E.
*1889 Swift, Edwin E.
1927 Swift, Harry P.
1916 Swift, Homer F.
1928 Swift, Walker E.
1926 Symmers, Douglas
*1888 Syms, Parker
1901 Synnott, Martin J.
1904 Taylor, Alfred S.
1922 Taylor, Charles G.
1901 Taylor, Fielding L.
1927 Taylor, Henry Keller
1898 Taylor, Howard C.
1930 Taylor, Howard C., Jr.
1933 Taylor, John Arthur
1920 Taylor, Kenneth
1932 Tenenbaum, Joseph
1925 Tenney, Charles F.
1927 Terry, Arthur H., Jr.
1918 Terry, Ira B., Jr.
1932 Tetelman, Michael M.
1911 Thacher, Henry C.
1910 Theobold, Carl
1890 Thomas, Allen M.
1924 Thomas, Joseph S.
1904 Thomas, William S.
1926 Thomasson, Aaron Hood
1927 Thomen, August A.
1929 Thompson, Charles Baker
1904 Thompson, Hugh C.
1929 Thompson, Samuel Alcott
1933 Thompson, William P.
1907 Thomson, John J.
1927 Thorburn, Grant
1908 Thorne, Victor C.
1922 Thornley, Josiah P.
1916 Throne, Binford
1931 Tickle, Thomas G.
1933 Tiebout, Harry Morgan
1910 Tieck, Gustav J. E.
1915 Tilney, Frederick
1901 Tilton, Benjamin T.
1906 Timme, Walter
1906 Titus, Edward C.
1913 Titus, Henry W.
1921 Titus, Norman E.
1922 Tobin, Thomas J.
1933 Tolmach, Jesse Alfred
1909 Tompkins, Walstein M.
1929 Toole, John
1891 Torek, Franz J. A.
1926 Touart, Maximin De M.
1931 Touroff, Arthur S. W.
1895 Tousey, Sinclair
1908 Tovey, David W.
1928 Tow, Abraham
1902 Townsend, Terry M

*Deceased

1933 Traeger, Cornelius Horace
1925 Traub, Eugene F.
1907 Travell, J. Willard
1932 Treves, Norman
1933 Trubek, Max
1917 Truesdell, Edward D.
1927 Tulipan, Louis
1929 Turner, Joseph
1906 Turnure, Percy R.
1932 Twinem, Francis Patton
1933 Twiss, John Russell
1919 Tyson, Cornelius J.
1890 Tyson, Henry H.
1933 Ulmar, David
1917 Unger, Arthur S.
1924 Unger, James Samuel
1927 Unger, Lester J.
1920 Urquhart, Howard D.
1912 Valentine, Julius J.
1910 van Beuren, Frederick T., Jr.
1906 Van Cott, Joshua M.
1927 Vander Veer, Albert, Jr.
1924 Van Derwerker, Earl E.
1931 Van Dyck, Laird S.
1922 Van Etten, Nathan B.
1920 Van Etten, Royal C.
*1927 Van Fleet, J. Flandreau
1906 Van Ingen, Philip
1932 Van Orden, Thomas D.
1906 Van Wagenen, Cornelius D.
1908 Vaughan, Harold S.
1932 Vero, Frank
1926 Verplanck, Van Noyes
1916 Vietor, John A.
1930 Vinciguerra, Michael
1890 Vineberg, Hiram N.
1914 Virden, John E.
1913 Vogel, Karl M.
1908 Vogeler, William J.
1903 Voislawsky, Antonie P.
1924 von Deesten, Henry T.
1927 von Glahn, William C.
1925 Von Sholly, Anna Irene
1928 Vorhaus, Martin G.
1931 Wachsmann, Siegfried
1931 Wade, Preston A.
1920 Wadhams, Robert P.
1927 Wagner, Lewis C.
1927 Waldie, Thomas E.
1928 Waldman, David P.
1904 Walker, Emma E.
1893 Walker, John B.
1903 Wallace, Charlton
1904 Wallace, George B.
1904 Wallace, Henry
1931 Wallace, Robert Pulley
1907 Wallhauser, Henry J. F.
1904 Walsh, James J.
1920 Walsh, Robert E.
1891 Walter, Josephine
1920 Walzer, Abraham
1933 Walzer, Matthew
1933 Warbasse, James P.
*1901 Ward, Freeman F.

*Deceased

1895 Ward, George Gray
1910 Ward, George H.
1908 Ward, Wilbur
1901 Ware, Martin W.
1932 Warren, Arthur Fulton
1914 Warren, Luther F.
1897 Warsaw, M. Claudius
1928 Warshaw, David
1925 Washburn, Arthur L.
1921 Washton, Jacob
1928 Watson, Benjamin P.
1920 Watson, Cassius H.
1932 Watson, William L.
1921 Webster, David H.
1932 Webster, Jerome P.
1919 Wechsler, Israel S.
1928 Weeden, Willis M.
1928 Weeks, Carnes
1886 Weeks, John E.
1920 Weeks, Webb W.
1922 Weil, Henry L.
1912 Weinstein, Harris
1927 Weintraub, Sydney
1932 Weiss, Harry
1930 Weissberg, Morris
1906 Welch, John E.
1909 Welker, Franklin
1894 Welt-Kakels, Sara
1933 Wertham, Frederic
1914 Wessler, Harry
1916 West, Davenport
1929 West, Randolph
1927 Westermann, John J., Jr.
1931 Wexler, David
1911 Wheeler, John M.
1928 Wheeler, Wm. L.
1926 Wheelwright, Joseph S.
1915 Whipple, Allen O.
1927 Whisenant, John R.
1911 White, Francis W.
1920 White, James W.
1882 White, John Blake
1920 White, William C.
1906 Whiting, Frederick
1920 Whitman, Armitage
1891 Whitman, Royal
1927 Whittemore, W. Laurence
1904 Wiener, Alfred
1914 Wiener, Herbert J.
1900 Wiener, Joseph
1883 Wiener, Richard G.
1908 Wiener, Solomon
1918 Wiggers, August F. A.
1905 Wightman, Orrin S.
1907 Wilcox, Herbert B.
1927 Wile, Ira S.
1927 Wilens, Ira
1914 Wilensky, Abraham O.
1927 Wilhelm, Seymour F.
1922 Willard, Luvia Margaret
1893 Willard, Thomas H.
1901 Williams, Anna W.
1903 Williams, Charles M.
1918 Williams, Frankwood E.
1916 Williams, Horatio B.
1928 Williams, Jesse F.
1904 Williams, Linsly R.
1886 Williams, Mark H.
1923 Williams, Percy H.
1905 Williams, William R.
1928 Williamson, Carolyn Gay

1918 Williamson, Hervey C.
1927 Willis, Benedict P.
1931 Wilmoth, Clifford Lee
1905 Wilner, Anna S.
1918 Wilson, Arthur S.
1900 Wilson, Frederic N.
1932 Wilson, Margaret Barclay
1917 Wilson, May G.
1914 Wing, Lucius A.
1927 Winkelstein, Asher
1909 Wise, Fred
1928 Wishner, Joseph G.
1924 Witt, Dan Hiter
1927 Woglom, William H.
1922 Wolf, Charles
1922 Wolf, George D.
1912 Wolf, Heinrich Franz
1899 Wolff, Julius
1931 Wollner, Anthony
1901 Wollstein, Martha
1911 Wood, Francis C.
1931 Wood, Paul M.
1924 Wood, Thomas D.
1910 Woodruff, I. Ogden
1917 Woodruff, Stanley R.
1927 Woodruff, W. Stuart
1928 Woody, McIver
1904 Woolley, Scudder J.
1891 Woolsey, George
1896 Wootton, Herbert W.
1917 Worcester, James N.
1932 Wortis, S. Bernard
1917 Wright, Arthur M.
1932 Wright, Irving Sherwood
1926 Wurtzel, George L.
1932 Wurzbach, Frederick A., Jr.
1918 Wyckoff, John H.
1910 Wyeth, George A.
*1889 Wylie, Robert H.
1932 Yaguda, Asher
1908 Yeomans, Frank C.
1910 Young, Anna R.
1910 Young, Charles H.
1928 Yudkowsky, Peter
1908 Zabriskie, Edwin G.
1921 Zadek, Isadore
1930 Zeiss, Robert F.
1927 Ziegler, Jerome M.
1932 Zilboorg, Gregory
1933 Ziporkes, Joseph
1909 Zipser, Jacques E.
1932 Zucker, Morris

Resident Members

Cipollaro, Anthony C.
Ginzburg, Leon
Grace, Arthur William
Martin, Hayes E.
Rappaport, Israel
Schwartz, Alfred A.

*Deceased

Non-Resident Fellows

1923 Ackerman, James F., Asbury Park, N. J.
1906 Adler, Herman M., Berkeley, Calif.
1903 Adriance, Vanderpoel, Williamstown, Mass.
1931 Ager, Louis C., Rutland Heights, Mass.
1881 Allen, Thomas H., Lake Mahopac, N. Y.
1898 Alling, Arthur N., New Haven, Conn.
1931 Anderson, Alan R., Freeport, L. I., N. Y.
1888 Armstrong, Samuel T., Katonah, N. Y.
1932 Atkinson, Walter S., Watertown, N. Y.
1882 Bacon, Gorham, Yarmouthport, Mass.
1904 Baker, S. Josephine, Stamford, Conn.
1916 Baldwin, Edward R., Saranac Lake, N. Y.
*1906 Barnum, Merritt W., Ossining, N. Y.
1914 Baughman, William H., Oakland, Calif.
1931 Bedell, Arthur J., Albany, N. Y.
1921 Benson, Arthur W., Troy, N. Y.
1920 Bibby, Henry L., Kingston, N. Y.
1908 Black, John Fielding, White Plains, N. Y.
1920 Blaisdell, Russell E., Orangeburg, N. Y.
1918 Blake, Eugene M., New Haven, Conn.
1895 Blake, Joseph A., Tucson, Ariz.
1924 Blancard, William, Roxbury, Conn.
1908 Blumer, George, New Haven, Conn.
1884 Boldt, Hermann J., White Plains, N. Y.
1927 Boltz, Oswald H., Binghamton, N. Y.
1919 Bonnell, Clarence H., Rye, N. Y.
1930 Booth, Arthur Woodward, Elmira, N. Y.
1897 Booth, Burton S., Troy, N. Y.
1931 Bourke, Victor G., Livingston Manor, N. Y.
1916 Bradbury, Samuel, Philadelphia, Pa.
1929 Branham, Vernon, Albany, N. Y.
1888 Brannan, John W., Camden, S. C.
1900 Brooks, Frank T., Litchfield, Conn.
1897 Brouner, Walter B., Asbury Park, N. J.
1907 Brown, David Chester, Danbury, Conn.
1915 Brown, Lawrason, Saranac Lake, N. Y.

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*Deceased

1922 Brown, Sanger, 2nd, Albany, N. Y.
1905 Brownlee, Harris F., Danbury, Conn.
1917 Caples, Byron H., Reno, Nev.
1928 Cattell, Henry W., Burlington, N. J.
1923 Cavanaugh, Thomas E., Springfield, Mass.
*1906 Chapman, Charles F., Mt. Kisco, N. Y.
1928 Cheever, Austin W., Boston, Mass.
1905 Chisholm, William A., Nova Scotia, Canada.
1911 Chittenden, Arthur S., Binghamton, N. Y.
1925 Christensen, Frederick C., Racine, Wis.
1930 Clarke, Thomas Wood, Utica, N. Y.
1885 Coe, Henry C., Washington, D. C.
1917 Cofer, Leland E., Palm Beach, Fla.
1907 Conaway, Walt P., Atlantic City, N. J.
1913 Conley, Walter H., Abroad.
1904 Connell, Karl, Wintoon Lodge, Branch, N. Y.
1920 Corbusier, Harold D., Plainfield, N. J.
1887 Currier, Charles G., Bernardsville, N. J.
1932 Currier, Gilman Sterling, Bernardsville, N. J.
1906 Curry, Grove P. M., Mt. Kisco, N. Y.
1929 Cutler, Max, Chicago, Ill.
1922 Cutter, William D., Chicago, Ill.
1933 Dalldorf, Gilbert J., Valhalla, N. Y.
1913 Davis, Fellowes, Jr., Paris, France.
1911 Day, Fessenden L., Bridgeport, Conn.
1879 De Garmo, William B., Coral Gables, Fla.
1911 Derby, Richard, Oyster Bay, L. I., N. Y.
1904 Divine, Alice, Ellenville, N. Y.
*1884 Dixon, George A., Paris, France.
1930 Doan, Charles Austin, Columbus, Ohio.
1895 Dobson, William G., Poughkeepsie, N. Y.
1926 Dowling, J. Ivimey, Albany, N. Y.
1924 Dye, John Sinclair, Waterbury, Conn.
1920 Eaton, Henry Douglas, Los Angeles, Calif.
1890 Edgar, J. Clifton, Greenwich, Conn.
1906 Estes, William L., S. Bethlehem, Pa.
1923 Farnell, Frederick J., Providence, R. I.
*1885 Farrington, William H., Raubsville, Pa.

*Deceased

1922 Fauntleroy, Archibald M., Ossining, N. Y.
1928 Finch, Lew Henri, Amsterdam, N. Y.
1911 Fitz, George W., Peconic, L. I., N. Y.
1912 Fitzgerald, Clara P., Worcester, Mass.
1894 Flint, Austin, Milbrook, N. Y.
1919 Flynn, Thomas J., Brooklyn, N. Y.
1913 Garcin, Ramon D., Richmond, Va.
1920 Gardner, Charles W., Bridgeport, Conn.
1922 Garvin, William C., Binghamton, N. Y.
1932 Gillette, David F., Syracuse, N. Y.
1929 Godfrey, Edward S., Jr., Albany, N. Y.
1897 Graves, Wm. B., Southport, Conn.
1908 Greenway, James C., New Haven, Conn.
1932 Gregg, Donald, Wellesley, Mass.
1901 Griffith, Frederic, Belmar, N. J.
1927 Haggart, Gilbert E., Boston, Mass.
1896 Hallock, Frank K., Cromwell, Conn.
1932 Hamilton, Samuel W., White Plains, N. Y.
1920 Hammond, Robert B., White Plains, N. Y.
1921 Harvey, Samuel Clark, New Haven, Conn.
1897 Haynes, Irving S., Plattsburg, N. Y.
1913 Hebert, Paul Z., Los Angeles, Calif.
1921 Heddens, Vernon O., Pasadena, Calif.
1910 Henderson, Alfred C., Stamford, Conn.
1911 Herring, Robert A., Washington, D. C.
1915 Hicks, Horace M., Amsterdam, N. Y.
1915 Hill, Miner C., Oyster Bay, L. I., N. Y.
1933 Hirshfeld, Samuel, Los Angeles, Calif.
1915 Holding, Arthur F., Albany, N. Y.
1927 Holters, Otto R., Asbury Park, N. J.
1915 Howland, De Ruyter, Stratford, Conn.
1918 Huffman, Otto V., Mt. Kisco, N. Y.
1916 Hughes, Frederic J., Plainfield, N. J.
1923 Hutchison, Fred R., Huntingdon, Pa.
1903 Hyde, Fritz Carleton, Dennis, Mass.
1933 Ivins, William Clifford, Trenton, N. J.
1933 Jameison, Gerald Reid, White Plains, N. Y.
1931 James, Bart Mulford, Bernardsville, N. J.
1908 Jameson, James W., Concord, N. H.

1912 Jean, George W., Santa Barbara, Calif.
1918 Jenison, Nancy, Bound Brook, N. J.
1906 Kann, Ulysses S., Binghamton, N. Y.
1925 Kempf, Edward John, Wading River, L. I., N. Y.
1895 Kilham, Eleanor B., Beverly, Mass.
1927 Klein, Alvin W., Stockbridge, Mass.
1932 Krieger, William Andrew, Poughkeepsie, N. Y.
1927 Kutil, Henry R., Huntington, L. I., N. Y.
1916 Lambert, Robert A., Paris, France.
1931 Lane, Clarence Guy, Boston, Mass.
*1916 Lane, John E., New Haven, Conn.
1912 Lathrope, George H., Morristown, N. J.
1923 Lawrence, Watson A., White Plains, N. Y.
1926 Lawton, Richard John, Terryville, Conn.
1896 Leach, Philip, U. S. N.
1910 Leake, James Payton, Washington, D. C.
1926 Leshin, Hiram R., Port Chester, N. Y.
1924 Levinson, Bernard, Freeport, L. I., N. Y.
1912 Longcope, Warfield T., Baltimore, Md.
1894 Lowe, Russell W., Ridgefield, Conn.
1904 Lynch, Robert J., Bridgeport, Conn.
1927 MacAusland, W. Russell, Boston, Mass.
1909 MacCallum, William G., Baltimore, Md.
1924 McCann, William S., Rochester, N. Y.
1908 McGavock, Edward P., Richmond, Va.
1928 McGraw, Arthur B., Detroit, Mich.
1920 Mackenzie, George M., Cooperstown, N. Y.
1931 McKiernan, Robert L., New Brunswick, N. J.
1885 McKim, W. Duncan, Washington, D. C.
1920 Maddren, William H., Stamford, Conn.
1931 Madill, Grant C., Ogdensburg, N. Y.
1928 Marcoglou, Angelos E., Athens, Greece.
1899 Marvel, Philip I., Atlantic City, N. J.
1884 Mendelson, Walter, Philadelphia, Pa.
1923 Mendez, Albert A., Punta San Juan, Cuba.
1919 Mendillo, Anthony J., New Haven, Conn.
1920 Merriman, M. Heminway, Waterbury, Conn.
1926 Messing, Arnold, Newburgh, N. Y.

*Deceased

1926 Metzger, Jeremiah H., Tyrone, N. M.
1905 Meyer, Adolf, Baltimore, Md.
1907 Mial, L. Le May, Morristown, N. J.
1900 Miles, Henry S., Bridgeport, Conn.
1927 Miller, John, Greenwich, Conn.
1933 Morgan, Audrey Goss, Washington, D. C.
1912 Morgan, William Gerry, Washington, D. C.
1921 Morrissey, Michael J., Hartford, Conn.
1931 Morse, Russell Wright, Minneapolis, Minn.
1916 Mott, Walter W., White Plains, N. Y.
1930 Mullins, Samuel F., Danbury, Conn.
1892 Munger, Carl E., Waterbury, Conn.
1918 Munn, Aristine P., West Long Branch, N. J.
1927 Murray, Henry A., Jr., Boston, Mass.
1932 Nelms, Homer L., Albany, N. Y.
1916 Neuman, Leo H., Albany, N. Y.
1923 Neumann, Theodore W., Central Valley, N. Y.
1902 Nicoll, Matthias, Jr., Rye, N. Y.
*1897 Nisbet, James D., Van Wyck, S. C.
1913 Ober, George E., Bridgeport, Conn.
1906 Oertel, Horst, Montreal, Canada.
1910 Oppenheimer, Frederick G., San Antonio, Texas.
1897 Orleman-Robinson, Daisy M., Meridale, N. Y.
1927 Overton, Frank, Patchogue, L. I., N. Y.
1919 Painter, Henry McM., Paris, France.
1912 Parker, Edward O., Greenwich, Conn.
1932 Parran, Thomas, Jr., Albany, N. Y.
1894 Parry, Angenette, Boston, Mass.
1909 Parry, Eleanor, Huntington, L. I., N. Y.
1893 Paton, Stewart, Baltimore, Md.
1910 Pearson, Henry, Center Conway, N. H.
1919 Pellini, Emil J., Peekskill, N. Y.
1923 Penfield, Wilder G., Montreal, Canada.
1922 Perkins, C. Winfield, Norwalk, Conn.
1921 Philips, Carlin, Miami, Fla.
1924 Phillips, Frank L., New Haven, Conn.
1896 Pierson, Samuel, Stamford, Conn.
1898 Pilgrim, Charles W., Central Valley, N. Y.

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*Deceased

1904 Pinkham, Edward W., Sarasota, Fla.
1926 Purdy, Sylvanus, White Plains, N. Y.
1889 Quinlan, Francis J., Amawalk, N. Y.
1922 Rainey, John J., Troy, N. Y.
1919 Raynor, Mortimer W., White Plains, N. Y.
1909 Reid, George C., Rome, N. Y.
1930 Reifenstein, Edward C., Syracuse, N. Y.
1928 Reilly, Thomas F., Springfield, Mass.
1916 Reynolds, Harry S., Hartford, Conn.
1921 Richardson, Henry B., Darien, Conn.
1932 Richardson, Ralph A., Bristol, Conn.
1905 Riggs, Austen Fox, Stockbridge, Mass.
1917 Robert, Daniel R., New Lebanon Center, N. Y.
1925 Roberts, Edward R., Bridgeport, Conn.
1904 Robertson, Joseph A., Dallas, Tex.
1901 Robinovitch, Louise G., Golden, Colo.
1920 Robinson, Horace Eddy, Pleasantville, N. Y.
1924 Rooney, James Francis, Albany, N. Y.
1894 Root, Edward K., Hartford, Conn.
1931 Ross, William H., Brentwood, L. I., N. Y.
1896 Rushmore, Edward C., Tuxedo Park, N. Y.
1920 Russell, Thomas Hubbard, New Haven, Conn.
1927 Russell, William L., White Plains, N. Y.
1913 Russell, Worthington S., Woodbury Falls, Orange Co., N. Y.
1928 Ryder, Morton, Rye, N. Y.
1905 Sadlier, James E., Poughkeepsie, N. Y.
1907 Sauer, J. George, St. Petersburg, Fla.
1927 Savarese, Melchior F. R., Orange, Conn.
*1893 Schauffler, William G., Princeton, N. J.
1896 Schavoir, Frederick, Stamford, Conn.
1922 Schwatt, Herman, Sanatorium, Colo.
1914 Scofield, Raymond B., Olmstedville, N. Y.
1911 Scruton, William A., Abroad.
1914 Seff, Isadore, Miami, Fla.
1929 Shamaskin, Arnold, Bedford Hills, N. Y.
1904 Sharp, Edward A., Buffalo, N. Y.
1926 Sheahan, William L., New Haven, Conn.

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*Deceased

1925 Simpson, Charles A., Washington, D. C.
1915 Slocum, Harry B., Long Branch, N. J.
1909 Smart, Isabelle T., Manasquan, N. J.
1914 Smith, Dorland, Bridgeport, Conn.
1908 Smith, E. Terry, Hartford, Conn.
1927 Smith, Ernest B., Philadelphia, Pa.
1909 Smith, George Milton, Pine Orchard, Conn.
1921 Smith, Scott L., Poughkeepsie, N. Y.
1920 Snyder, William H., Newburgh, N. Y.
1908 Sorapure, Victor E., London, England.
1894 Spence, Daniel B., Holmes, Dutchess Co., N. Y.
1914 Sperry, Frederick N., New Haven, Conn.
1933 Sprague, George S., White Plains, N. Y.
1932 Standish, E. Myles, Hartford, Conn.
1933 Steiner, Walter, Hartford, Conn.
1915 Stone, Harry Russell, Clinton, Conn.
1909 Storey, Thomas A., Stanford Univ., Calif.
1912 Stover, Charles, Amsterdam, N. Y.
1907 Stratton, Edward A., Danbury, Conn.
1929 Strauss, Maurice J., New Haven, Conn.
1913 Strobell, Charles W., San Diego, Calif.
1933 Sutherland, Francis A., New Haven, Conn.
1917 Sweet, Charles C., Ossining, N. Y.
1932 TenBroeck, Carl, Princeton, N. J.
1918 Terry, Benjamin T., Tacoma, Wash.
1918 Thoms, Herbert, New Haven, Conn.
1895 Toms, S. W. Spencer, Nyack, N. Y.
1924 Tooker, Harold Clifton, Springfield, Mass.
1928 Torrey, Harry Beal, Palo Alto, Calif.
1932 Trible, George Barnet, Washington, D. C.
1923 Turrell, Guy H., Smithtown Branch, L. I., N. Y.
1916 Vander Bogert, Frank, Schenectady, N. Y.
1902 Van Vranken, Gilbert, Altadena, Calif.
1928 Vessie, Percy R., Ossining, N. Y.
1924 Vier, Henry John, White Plains, N. Y.
1896 Vietor, Agnes C., Boston, Mass.
1905 von Tiling, Johannes H. M. A., Poughkeepsie, N. Y.
1931 Voss, Fred H., Kingston, N. Y.
1907 Wadsworth, Augustus B., Albany, N. Y.
1918 Wahlig, Herman G., Sea Cliff, Nassau Co., N. Y.

the pathogenesis of diabetic hyperpyrexia. In order to imitate this polyuria which for our purposes consists chiefly of a loss of water and salt it was necessary simply to withhold insulin from the depancreatized dogs. The high blood sugar following this procedure produced a polyuria, a loss of fluids from the body. To accentuate and intensify the loss of fluids not only insulin but also water was withheld from the diabetic animals.

You may well imagine our pleasure when this simple technique resulted in the production of marked fever in our experimental animals. Indeed, it was possible to produce fever of more than 104° F. with striking ease and regularity and it is the functional pathology and clinical features of this fever which I desire to present to your attention this evening.

That the simple procedure of withholding insulin and water reduces the volume of the circulating blood can be seen in the following table. Here it will be observed that the specific gravity of the blood serum rose from 1.0251 to 1.0309 during a period of three days, while the temperature rose from 100.9 to 105.3.

TEMPERATURE AND SPECIFIC GRAVITY DURING DIABETIC HYPERPYREXIA

Water Intake	Temp. °F	Specific Gravity of Serum
Ad. Lib.	100.9	1.0251
None for 9 hours...........	102.2	1.0277
None for 24 hours..........	105.3	1.0309

The great increase in the specific gravity of the serum determined by the method of Barbour and Hamilton (1926) indicates that the water content of the blood has been correspondingly diminished—that there is an anhydremia. The specific gravity is an indicator of the amount of solids in the blood. As solids increase there is a proportional decrease in the water content. Certainly, in this experiment the anhydremia increased along with the tem-

1922 Cooke, Elizabeth, Stamford, Conn.
1925 Corwin, E. H. L., New York.
1930 Dakin, Henry D., Scarborough-on-Hudson, N. Y.
1910 Davenport, Charles B., Cold Spring Harbor, N. Y.
1930 Detwiler, Samuel R., New York.
1933 Dunbar, Helen Flanders, New York.
1928 Dunning, William B., New York.
1920 Fine, Morris S., Battle Creek, Mich.
1927 Flinn, Frederick B., New York.
1926 Folks, Homer, New York.
*1927 Franken, Sigmund W. A., New York.
1930 Fry, Henry J., New York.
1928 Gies, William J., New York.
1932 Goebel, Walther F., New York.
1932 Goldforb, Abraham J., New York.
1927 Green, Leo, New York.
1914 Greenwald, Isidor, New York.
1911 Harris, Isaac F., Tuckahoe, N. Y.
1928 Hartman, Leroy L., New York.
1930 Hellman, Milo, New York.
1930 Hirschfeld, Isador, New York.
1930 Holmes, Joseph L., New York.
1932 Kahn, Morton C., New York.
1927 Kingsbury, John A., New York.
1930 Kleiner, Israel S., Brooklyn.
1928 Kopeloff, Nicholas, New York.
1923 Krasnow, Frances, New York.
1932 Landis, Carney, New York.
1905 Lee, Frederic S., New York.
1921 Little, Clarence C., New York.
1928 McCaffrey, Francis S., New York.
1931 McFarland, Ross A., New York.
1926 Miller, Edgar Grim, Jr., New York.
1928 Myers, Chester N., Yonkers, N. Y.
1923 Myers, Victor C., Cleveland, Ohio.
1927 Neuwirth, Isaac, New York.
1928 Noback, Gustave J., New York.
1932 Northrop, John H., Princeton, N. J.

*Deceased

1927 Oppenheimer, Enid Muriel, New York.
1932 Osterhout, W. J. V., New York.
1928 Palmer, Bissell B., New York.
1927 Paulsen, Alice E., Bronxville, N. Y.
1931 Paynter, Richard H., Brooklyn.
1929 Renshaw, Raemer Rex, New York.
1927 Scott, Ernest L., New York.
1918 Seaman, Emily C., New York.
1931 Shuman, Harry Benjamin, Boston.
1928 Smith, Bertram G., New York.
1929 Smith, Homer Wm., New York.
1928 Sobotka, Harry H., New York.
1904 Soper, George A., Great Neck, L. I., N. Y.
1926 Strong, Oliver Smith, New York.
1930 Sydenstricker, Edgar, New York.
1928 Tallman, Gladys G., New York.
1928 Torrey, John C., New York.
1927 Tracy, William D., New York.
1932 Van Slyke, Donald D., New York.
1928 von Wedel, Hassow O., Ardsley-on-Hudson, N. Y.
1927 Waugh, Leuman M., New York.
1927 Weinberger, Bernhard W., New York.

Associates

Bellows, Marjorie T., White Plains.
Fischer, Robert Morris, New York.
Schweitzer, Jerome M., New York.

Recapitulation

	Number
Resident Fellows & Members	1,674
Non-Resident Fellows & Members	234
Associate Fellows & Associates	78
Fellows on Exempt List	175
Fellows on Teaching or Research List	119

Honorary Fellows

Abel, John Jacob, ScD., LL.D. Baltimore.
Achard, Charles, M.D., Paris.
Alessandri, Roberto, M.D. Rome.
Archibald, Edward William, M.D. Montreal.

Ballance, Sir Charles, C.B., M.V.O., LL.D., M.S., F.R.C.S. London.
Banting, Frederick Grant, M.C., M.D., F.R.C.S., Ds.C., LL.D. Toronto.
Barany, Robert, M.D. Upsala, Sweden.
Bastianelli, Raffaele, M.D. Rome.
Bordet, Jules, M.D. Brussels.
Chagas, Carlos. Rio de Janeiro.
Chittenden, Russell Henry, Ph.B., Ph.D., LL.D. New Haven.
Curie, Marie Sklodowska, D.Sc. Paris.
Cushing, Harvey W., M.D., Sc.D., LL.D., F.R.C.S., D.S.M. New Haven.
Dale, Sir Henry Hallett, C.B.E., M.A., M.D., F.R.S., F.R.C.P. London.
de Schweinitz, George E., M.D., LL.D. Philadelphia.
Dock, George, M.D., ScD. Pasadena.
Farrand, Livingston, M.D., LL.D. Ithaca.
Finney, John M. T., M.D., F.R.C.S., D.S.M. Baltimore.
Foerster, Otfried, M.D. Breslau.
Forssell, Carl G., M.D. Stockholm.
Fournier, Alfred, M.D. Paris.
Head, Sir Henry, M.D., F.R.C.P., LL.D., F.R.S. London.
Herrick, James Bryan, M.D. Chicago.
Hopkins, Sir Frederick Gowland, M.B., D.Sc., LL.D., F.R.C.P., F.R.S. Cambridge.
Jackson, Chevalier, M.D. Philadelphia.
Jadassohn, Josef, M. D. Breslau.
Kappers, Cornelius Ubbo Ariens, M.D. Amsterdam.
Kitasato, S., M.D. Tokio.
Leriche, René, M.D., D.Sc. Strasbourg.
Lewis, Sir Thomas, C.B.E., M.D., F.R.C.P., D.Sc., F.R.S. London.
Marie, Pierre, M.D. Paris.
Martin, Sir Charles James, C.M.G., M. B., D. Sc., LL.D., F.R.S. London.
Matas, Rudolph, M.D., LL.D., F.A.C.S. New Orleans.
Minot, George Richards, M.D. Brookline.
Moynihan, Rt. Hon. Lord Berkeley, K.C.M.G., C.B., LL.D., M.S., F.R.C.S. Leeds.

Neufeld, Friedrich, M.D. Berlin.
Newman, Sir George, K.C.B., M.D., D.C.L., LL.D. London.
Pavlov, Ivan Petrovic, M.D. Leningrad.
Putti, Vittorio, M.D. Bologna.
Ramón y Cajal, Santiago, M.D. Madrid.
*Roux, Emile, M.D. Paris.
Sherrington, Sir Charles S., O.M., G.B.E., M.D., LL.D., F.R.S. Oxford.
Smith, Theobald, M.D., Sc.D. Princeton.
Spiller, William Gibson, M.D. Philadelphia.
Vogt, Alfred, M.D. Zurich.
von Müller, Friedrich, M.D. Munich.
Welch, William Henry, A.B., M.D., LL.D. Baltimore.
Wenckebach, Frederick Karel, M.D. Vienna.

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Attention is directed to the following extract from the will of Mrs. Celine B. Hosack:

"I do give and bequeath unto my executors, hereinafter named, the sum of Ten Thousand Dollars, in trust to apply and pay the same (or so much thereof as may be necessary) to The Roosevelt Hospital in the City of New York, to purchase a bed which, in memory of my husband, shall be known as the Hosack Bed, and which shall be occupied from time to time by such sick and needy physicians as may for that purpose be named or designated by the President and Treasurer for the time being of The New York Academy of Medicine."

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FORM OF BEQUESTS

The following is a brief legal form as a suggestion under which bequests may be made in behalf of the Academy:

I give, devise and bequeath unto "The New York Academy of Medicine" of the City of New York, State of New York, a corporation duly incorporated by the Legislature of the State of New York by an act entitled, "An Act to Incorporate The New York Academy of Medicine," passed June 23, 1851, and amended June 4, 1853, June 2, 1877, and April 25, 1924, . . .

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FLUID DISTRIBUTION AND EDEMA*

A. Ashley Weech

The student of equilibria in physiology will be impressed by a trend of thought in modern attempts to understand so-called "disturbances of balance". The human organism is coming to be regarded as a unit. It is recognized that in health the proper function of each part is dependent on normal function of a number of other parts, that a given symptom is rarely caused entirely by defect of a single organ, but results more commonly from numerous interrelated happenings in different regions of the body. Such a conception is essential for this evening's lecture "fluid distribution and edema". It will be necessary to examine data concerning a number of different factors or conditions which are involved in maintaining normal distribution or in promoting abnormal accumulation of fluid in the tissues. We must further attempt to discover in which manner the various factors are interrelated.

* Delivered October 26, 1933.

To facilitate orderly discussion I have tabulated the factors to be dealt with (Table 1). It may be assumed

TABLE 1.

THE REGULATION OF FLUID DISTRIBUTION IN THE BODY

A. FACTORS OPERATING AT THE WALL OF THE CAPILLARY.
1. Colloid osmotic pressure of the plasma.
2. Capillary blood pressure.
3. Colloid osmotic pressure of tissue fluid.
4. Mechanical pressure in the tissue spaces.
5. Permeability of the capillary wall.

B. FACTORS WHICH MODIFY THE FORCES ON THE OUTSIDE OF THE WALL OF THE CAPILLARY.
1. Lymph flow.
2. Elasticity of the tissues.

C. FACTORS WHICH MODIFY THE FORCES ON THE INSIDE OF THE WALL OF THE CAPILLARY.
1. Excessive proteinuria.
2. Protein starvation.
3. Venous obstruction and cardiac stasis.
4. Variations in salt intake.
5. The kidney.

to be axiomatic that fluid reaches the tissues by way of the blood stream, that is, by passing through the walls of the capillaries. For this reason the forces which govern the movement of fluid across the capillaries will be regarded as fundamental in controlling fluid distribution and I have grouped them together under "A". It is none the less true that the fundamental forces may be subject to modification from change in remote regions of the body and that the remote changes will often be the primary cause of disturbance. To consider all possible remote influences comprehensively would require far more time than is available and at the same time, because present knowledge is incomplete, be of dubious value. Those which I have placed under "B" and "C" have been selected because at the moment they seem to possess an importance deserving of emphasis. They include factors which modify the forces on the outside of the wall of the capillary and other factors which it is believed exert their effect on the forces within the capillary.

Our discussion may be opened suitably with two diagrams, introduced to make clear the action of osmotic forces in general. The test-tube-like structure in the first diagram (Fig. 1.) represents a membrane which may be com-

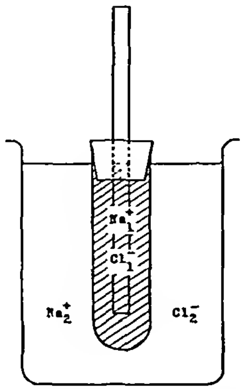

Fig. 1. Osmotic system in which only salts are present for which the membrane is permeable. No pressure is developed.

posed of collodion, parchment, or some similar substance. At the outset one concentration of sodium chloride is placed on the inside of the membrane and another concentration on the outside. The system is closed and connected to a manometer which can record any pressure within the membrane. The final state of affairs is depicted when the membrane permits the free passage of both sodium and chloride ions. By diffusion the concentrations of the two solutions are equalized and no osmotic pressure is developed. The final state is different (Fig. 2.) when within the membrane there is an additional large ion or molecule (R) which is unable to pass the membrane wall. Because the molecule cannot diffuse, ultimate equality of concentration on the two sides of the membrane is impossible and an osmotic pressure is developed, the magnitude of which is revealed by the height of the water column in the manometer. It is important to note that the osmotic pressure recorded by the system is independent of the concentrations of sodium and chloride and depends only on the concentration of R, that is, the molecule for which the membrane is impermeable.

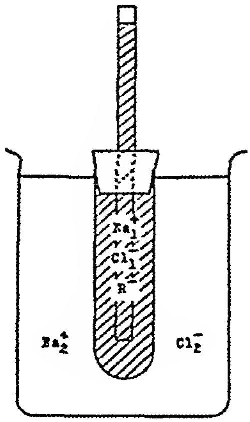

Fig. 2. Osmotic system in which there is present an additional molecule "R" for which the membrane is impermeable. Pressure is developed and measured by the height of the water column in the manometer.

A system similar to this one exists across the membrane wall of the capillaries which separate the blood plasma from interstitial fluid. The capillary is freely permeable to all of the substances dissolved in blood with the excep- *tion of protein which, therefore, exerts an osmotic pressure* which endeavors to draw fluid from the tissue spaces into the blood stream. The total osmotic pressure of all the plasma crystalloids (sodium, potassium, bicarbonate, chloride, urea, etc.) lies between 5000-6000 mm. of mercury, that of the plasma colloid (protein) is normally from 20-30 mm. of mercury. Nevertheless, the property of free diffusion prevents the development of pressure due to crystalloids and only the colloid osmotic pressure is concerned in water distribution. Colloid osmotic pressure may be measured directly on samples of plasma outside the body by the use of a system containing a semipermeable brane. It can also be calculated from the protein concentration of the plasma. For this purpose a knowledge of the total protein content is of little value. In chemical constitution the albumin molecule is much smaller than that of globulin, and, therefore, gram for gram, albumin gives more osmotically active particles than globulin.

Govaerts has estimated that 1.0 gram of albumin per 100 c.c. will produce an osmotic pressure of 5.5 mm. of mercury, whereas a similar concentration of globulin produces a pressure of only 1.4 mm. of mercury. With a knowledge of the albumin and globulin fractions it is possible to make an approximate calculation of the colloid osmotic pressure. In practice, because the pressure of globulin is small, osmotic pressure will be found roughly to parallel albumin concentration and the latter figure, obtained by direct analysis, is sometimes used as a measure of this force. Nevertheless, it is well to remember that rare cases are occasionally encountered in which a very high figure for plasma globulin renders the pressure from this fraction more important than that of albumin.

Colloid osmotic pressure, then, due chiefly to plasma albumin, tends to draw fluids into the circulation. In the normal individual this force is counterbalanced by a factor which appeared second on our list, namely, blood pressure within the capillaries. This blood pressure depends upon the force of the heart beat, vessel elasticity and hydrostatic effects. I have reproduced here (Fig. 3.) a diagram

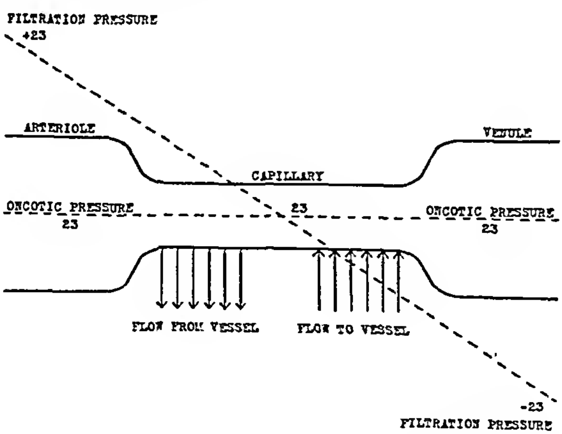

Fig. 3. The effect of mechanical pressure and colloid osmotic pressure on the flow of fluid through the wall of the capillary. After Christian (*J. A. M. A.*, 1931, *97:* 296).

taken from an article by Christian which may serve to illustrate the nicety with which the balance is maintained in health as well as the disturbances which lead to edema formation. The diagram portrays the course of events as blood flows from an arteriole, through a capillary, and into a venule. The dotted line running through the middle of the vessel indicates constancy of protein in the blood and, therefore, constancy of the colloid osmotic pressure, which in this instance is represented as having a normal value of 23 mm. of mercury. The diagonal dotted line indicates that mechanical blood pressure is falling as the blood continues its course through the capillary. On the arterial side of the capillary the pressure is seen to be greater than 23 mm. of mercury and on the venous side it is something less than 23 mm. A fall in pressure through this range is not an imaginary happening. Direct measurements by E. M. Landis of the pressure in single capillaries at the base of the human finger nail have shown that on the average the pressure falls from 32 mm. of mercury at the arterial end of the capillary to 12 mm. at the venous end. When we consider, then, the combined effect of the two opposing forces, it is seen that mechanical pressure is greater at the arterial side of the capillary and that osmotic pressure is greater at the venous side. The result will be, as is shown by the arrows, that fluid will first be expressed mechanically from the vessel and later returned by osmotic attraction. Such a to-and-fro flow of fluid has actually been demonstrated by Schade and Claussen on model capillaries constructed of collodion and perfused with normal serum. In health the balance between filtration and reabsorption is so nicely adjusted that no excess of free fluid can accumulate in the interstitial spaces. Such accumulation may, however, occur when the balance is disturbed. We shall see how this can be.

When a vein is obstructed mechanically or when generalized venous congestion has resulted from heart disease, a rise in pressure in the veins takes place which is reflected back into the capillaries. The rise in capillary blood pressure increases the filtering area of capillary wall

and decreases the resorptive area in such a way that more fluid leaves and less fluid returns to the vessel than under normal conditions. The disturbance brings about an increased accumulation of tissue fluid which, if great enough, will become manifest as palpable edema. A derangement of this sort is certainly one of the major factors in the production of cardiac edema.

On the other hand we are acquainted with several clinical diseases in which depletion of the blood protein and, therefore, of the plasma colloid osmotic pressure, is a conspicuous feature. The effect of the depletion is the same as an increase in mechanical pressure in bringing about a preponderance of filtration over reabsorption. If sufficient in degree it may also be the cause of edema. It can no longer be doubted that a major factor in the production of the edema of chronic Bright's disease is to be found in the plasma protein deficit which results from continued excessive proteinuria. There is also abundant evidence to show that prolonged protein starvation will lead to a similar depletion of the plasma protein and subsequently to edema. The relation between depleted plasma proteins and edema has been demonstrated by a number of investigators, chiefly by Dr. Peters and his colleagues in New Haven and by Drs. Moore and Van Slyke here in New York. It is shown clearly in Figure 4 in which have been charted some of our data concerning the relationship between plasma proteins and experimental edema in dogs. The black dots represent analyses of plasma made when edema was present and the open circles refer to estimations made before edema had developed or after it had disappeared. It is seen that edema rarely appeared before the albumin was depleted below 2 grams per 100 c.c., that it was more often present than absent when the albumin was between 1 and 2 grams per 100 c.c., and that below 1 gram edema was always present. The relative importance of albumin in controlling osmotic pressure is shown by the absence of any correlation between globulin and edema and by the relatively slight correlation between total protein and edema. Charts

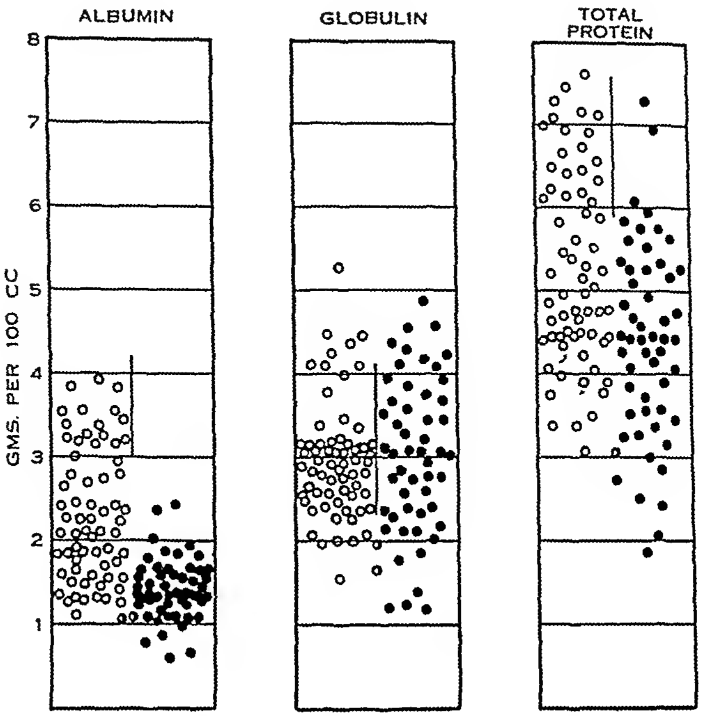

Fig. 4. The relation between plasma protein concentration and edema in dogs. Open circles indicate estimations made when no edema was present; black circles indicate estimations made when edema was present; vertical lines in the middle of each column indicate the range of normal variation. After Weech, A. A., Snelling, C. E., and Goettsch, E. (*J. Clin. Invest.*, 1933, *12*: 193).

similar to this may easily be prepared from data obtained on humans although with humans the level of albumin associated with the appearance of edema is somewhat higher than with dogs. According to Moore and Van Slyke it lies between 2.3 and 2.7 grams per 100 c.c.

It is seen, then, that disturbance of a balance between two opposing forces on the inside of the capillary may take place so as to favor edema formation. The credit for gnizing first the importance of this balance belongs Starling in 1896. The theory of Starling is concerned chiefly with forces arising within the capillary. It is now necessary to inquire whether extramural forces need not

also be considered in evaluating the movement and distribution of fluid. For it is possible to conceive of mechanical and osmotic forces within the tissue spaces as well as within the capillaries. Unfortunately exact knowledge of these forces is still fragmentary. It is pertinent, however, to observe that, when the balance between intracapillary forces is disturbed in such a way that filtration occurs in excess of resorption, fluid does not continue to enter the tissue spaces in unlimited quantities. It is apparent that distending the tissues with fluid creates a certain amount of back-pressure and that this in time compensates for the disturbed balance and leads to the establishment of a new equilibrium. The exact magnitudes of tissue pressure are yet unknown. It is certain that it cannot rise higher than capillary blood pressure for such an increase would lead to collapse of the vessels. Moreover, we shall see in a moment, that tissue pressure probably varies continuously during physical activity and approaches constancy only during complete rest. It may be stated, however, that the effective mechanical force operating across the wall of the capillary is not represented by capillary blood pressure alone but rather by the difference between this pressure and mechanical tension in the tissues. In an analogous manner we must suppose the effective osmotic pressure to be the difference between osmotic pressure on the inside and on the outside of the wall of the capillary. Again, however, we are faced by a paucity of information concerning the concentration of protein in tissue fluid for during health this fluid exists in such small amounts that it cannot be obtained for analysis and its composition is really unknown. Although it is true that so-called filtration edemas, such as occur in chronic nephritis and malnutrition, are characterized by an edema fluid of extremely low protein content, it is dangerous to infer from this finding that normal tissue fluid is to a like extent protein-free. Within the last few years Drinker and Field of Harvard have given reasons for their belief that lymph and tissue fluid possess "an approximate degree of identity" and have shown that lymph contains more protein than has

usually been supposed to exist in tissue fluid. Although there is not time in this place to enter upon a discussion of the relationship between these two fluids, it is likely that the protein content of normal tissue fluid is not negligible.

As an aid to visualization of the interplay between forces on both sides of the capillary wall, it is possible to express the relationship during periods of equilibrium, that is, at times when edema is neither advancing nor receding, in equation form:

$$S - I = C - T$$

During these periods the total forces on the inside of the capillary must equal those on the outside, a relationship which the equation expresses by representing the difference between the colloid osmotic pressure of serum (S) and the colloid osmotic pressure of tissue fluid (I) as equal to the difference between capillary blood pressure (C) and mechanical pressure within the tissues (T). We have already seen that a reduced osmotic pressure of serum or an increased blood pressure in the capillaries favors the filtration of more fluid toward the tissues. The equation indicates that a similar effect might result from an increase in the osmotic pressure of tissue fluid or from a decrease in tension within the tissues.

The protein content and, therefore, the colloid osmotic pressure, of tissue fluid are determined principally by the degree to which the capillaries are permeable to protein. In certain morbid processes the permeability may be greatly increased and an edema result in which the protein content of the edema fluid approaches that of the plasma. Allergic edema and the edema of inflammation belong in this group. The process is essentially a simple one in which blood plasma, as such, infiltrates the tissues. It is fundamentally different from that which gives rise to nephrotic edema, nutritional edema, or cardiac edema.
- deed, recently collected data suggest that those forms of
edem... in 18 haracterized by edema fluids of low pro-
chiefly with forces be associated with capillaries whose
necessary to inqui- to protein has been appreciably de-

creased rather than increased. If this is true, the edema has occurred in spite of changes in the capillary wall which might be looked on as an attempt at compensation. The evidence which has led us to this inference of decreased permeability of the capillaries in filtration edema may be presented briefly. Table 2 presents the protein concentra-

TABLE 2.

PROTEINS IN LYMPH AND SERUM OF NORMAL AND EDEMATOUS DOGS

Normal Animals				Edematous Animals			
Dog	Lymph Protein per cent	Serum Protein per cent	Serum Prot. / Lymph. Prot.	Dog	Lymph Protein per cent	Serum Protein per cent	Serum Prot. / Lymph. Prot.
841	1.92	6.83	3.6	992	0.07	2.10	30.0
842	2.93	7.40	2.5	6	0.39	2.60	6.7
895	0.74	5.60	7.6	58	0.11	2.49	22.6
949	1.25	6.04	4.8	840	0.13	2.88	22.2
950	3.45	7.89	2.3	91	0.46	3.32	7.2
100	0.66	5.70	8.6	23	0.17	3.38	19.9
58	0.90	5.70	6.3	5	0.22	3.24	14.7
69	1.26	5.77	4.6	131	0.04	3.20	80.0
91	1.89	6.38	3.4	838	0.37	3.00	8.1
92	1.40	5.73	4.1	806	0.36	3.00	8.3
131	1.17	5.99	5.1				
840	1.46	5.07	3.5				
Mean (Geometric)	1.41	6.13	4.4	Mean (Geometric)	0.18	2.89	16.1

tions of subcutaneous lymph and blood serum in a series of normal dogs which are to be compared with similar analyses in a group of edematous dogs. I may mention that the protein of lymph is derived from the blood and represents material which has filtered through capillaries. When the protein of serum decreases, other things being equal, we should expect a proportionate decrease in the protein of lymph. With the animals from which the figures in the table were derived the experimental procedure responsible for edema reduced the serum protein to about half its original value. The reduction in lymph protein, however, occurred at a much more rapid rate,

the mean value in the edematous animals being one-eighth that in the normal animals. The disproportionate reduction is likewise reflected in a striking rise in the ratio of serum protein to lymph protein. This change cannot be explained simply on the basis of an increase in filtration pressure but can be accounted for by supposing that a decline in the protein of serum is associated with a diminished permeability of the capillaries.

An analogous conclusion is suggested by the data presented in Table 3. When a cannula is introduced into one

TABLE 3.

FLOW OF LYMPH FROM THE EXTREMITIES OF DOGS AFTER ESTABLISHMENT OF CONSTANT RATE

Normal Animals			Edematous Animals		
Dog	Serum Osmotic Pressure mm. of Hg	Rate of Flow c.c. per 10 min.	Dog	Serum Osmotic Pressure mm. of Hg	Rate of Flow c.c. per 10 min.
91	24.3	0.6	58	8.9	0.4
100	17.6	0.7	992	6.7	0.6
92	18.5	1.1	6	9.6	1.1
840	19.8	1.5	6	9.6	1.3
131	21.6	1.6	992	6.7	1.4
58	22.1	4.8	840	7.6	1.7
			91	11.8	1.7
			131	10.4	2.4
			23	9.9	2.6
			58	8.1	3.0
			23	9.9	3.6
			5	10.1	5.3
Average	20.7 ± 0.6*	1.71 ± 0.39*	Average	9.1 ± 0.3*	2.09 ± 0.26*

*Probable error of mean.

of the peripheral lymphatics and the flow of lymph stimulated by keeping the extremity in motion, the rate of flow is at first variable but after a time becomes constant and

may remain so for several hours. During the period of constant flow the observed rate must correspond to the production of fresh lymph, that is, to the rate of capillary filtration in the extremity. In the table there have been recorded a number of examples of the rate of lymph flow when constancy was reached in both normal and edematous animals. The range of variation is seen to be approximately the same in the two groups, that is, between 0.6 and 4.8 c.c. per 10 minutes in the normal animals and between 0.4 and 5.3 c.c. per 10 minutes in the edematous animals. The average rate of flow for the edematous dogs is very slightly greater than for the normal dogs. The data for serum osmotic pressure show a reduction from 20.7 to 9.1 mm. of mercury; the reduction must have caused a considerable rise in filtration pressure, and we are forced to explain the failure to observe a significant increase in the rate of filtration from the capillary. The failure can be accounted for by assuming again that the reduction in serum proteins in the edematous animals has been accompanied by diminished capillary permeability and, therefore, by a restricted rate of capillary filtration.

Until now our discussion has dealt almost exclusively with forces and conditions controlling the filtration of fluid across the capillaries. We have noted in passing that remote influences such as protein starvation, excessive proteinuria, or cardiac stasis may disturb the balance of forces at the wall of the capillary and lead to edema. The manner of action of these influences is direct and relatively easily understood. We must now consider briefly several less apparent factors which may likewise modify conditions around the capillary.

Chief among the factors which control conditions on the outside of the capillary are the minute radicles of the lymphatic system. To understand their action it is necessary to bear in mind (1) that the radicles are as numerous and as diffusely distributed as the blood capillaries, (2) that their connection with the intercellular and intercapillary tissue spaces is most intimate, and (3) that they

possess no intrinsic mechanism for maintaining a continuous flow of fluid through their lumens. The lymphatics are abundantly supplied with valves which when massaged from the outside act as so many small pumps and establish an intermittent type of circulation which is active when the animal is moving and which ceases entirely during complete rest. At times of complete inactivity, therefore, fluid accumulates in the tissue spaces with a rise in tissue pressure until capillary filtration and reabsorption are equal and further accumulation is stopped. It is to this equilibrium of physical inactivity only that the equation expressing the balance between forces about the wall of the capillary applies. When the muscles are moved the lymphatics are activated at once, fluid is withdrawn from the tissue spaces with a corresponding fall in tissue pressure, and the balance around the capillary is disturbed so as to increase capillary filtration. A continuous circulation of fluid is thereby created from the capillary, through the tissue spaces, and into the lymphatics. From one point of view, then, the lymphatics can be looked upon as a major factor in controlling pressure within the tissue spaces and thereby indirectly influencing the volume of capillary filtrate. It is clear that tissue pressure cannot rise to a higher value than that necessary to render capillary reabsorption equal to filtration. It is likely, however, that more or less intermittent activity of the lymphatics serves constantly to maintain tissue pressure at values somewhat lower than the maximum.

Another important function is served by the lymphatics. We have seen that the capillaries are not completely impermeable to protein and it is evident that in the absence of some regulatory mechanism any degree of permeability, however slight, would in time lead to equilibrium of protein concentrations on the two sides of the membrane. For, in this case the constant diffusion of protein irrespective of the movement of fluid is concerned. The regulatory mechanism is supplied by the lymphatics which by removing fluid mechanically from the tissue spaces prevent the lapse of time necessary for equality of protein concen-

tration with the blood. The edema which results from lymphatic obstruction in all probability is not caused by the damming back of fluid in the tissues but rather results from the fact that the mechanism for maintaining a tissue fluid of relatively low protein content has been destroyed. The end result, an edema fluid of high protein content, is similar to that which develops when the permeability of the capillaries has been greatly increased by inflammatory disease. I may mention that the edema of tropical elephantiasis is supposed to result from blockage of the lymphatics with filariae and that Drinker and Field have succeeded in producing a chronic localized edema in dogs by utilizing an injection mixture containing quinine and powdered silica to obstruct the draining lymphatic trunks.

One other factor capable of modifying conditions on the outside of the capillary wall remains to be mentioned. I refer to the elasticity of the tissues themselves. We have seen that a change in the forces about the capillary in the direction which favors a preponderance of filtration over reabsorption is ultimately compensated by a rise in pressure in the tissue spaces. It is clear that the rise in pressure will create a stress which must be borne by the interstitial tissues and that no phenomenon of edema could exist if the tissues were incapable of yielding to increasing stress. Unfortunately little information exists concerning the manner whereby they do yield. It is certain that they are not perfectly elastic, that is, that equal increments of stress do not produce equal increments of stretching. The most recent work of Holland and Meyer would suggest that they are plastic in nature, exhibiting very slight elasticity under moderate stress, yielding suddenly to greater stress, and being unable to return immediately to the original state on withdrawal of the stress. The nature of this "tissue elasticity" is too obscure to warrant more lengthy discussion. It is mentioned because a change in its character would be expected to alter the distribution of fluid.

Two phenomena of great importance remain for discussion. Both are familiar to every clinician, both have contributed to our therapeutic armamentarium, both have been studied extensively on the ward and in the laboratory, and yet both are still shrouded in mystery for him who wishes to know "the how and the why". I refer to the hydropigenous action of salt on the edematous state and to the sudden occurrence of diuresis with loss of edema in nephrotic patients when analyses fail to indicate any significant increase in the proteins of the serum. Because our discussion must be brief I shall introduce the phenomena by presenting the results of one of our experiments with dogs.

Figure 5 presents the record of an animal which was

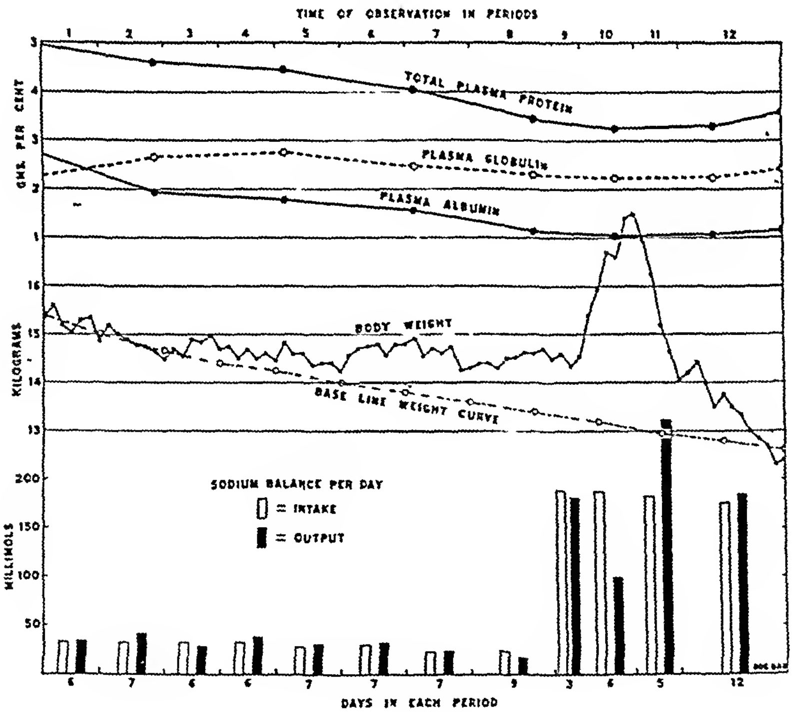

Fig. 5. Development of nutritional edema in a dog. The experiment reproduces two phenomena which are often observed in human patients—(1) marked retention of fluid following the ingestion of salt, and (2) spontaneous diuresis.

maintained 81 days on a diet deficient in protein. During the first 8 metabolism periods (55 days) the diet contained about 30 millimols of sodium chloride daily; for the remainder of the experiment the salt intake was increased to about 200 millimols daily. The diet is seen to have led to gradual lowering of the plasma albumin concentration. The broken line which is marked "Base Line Weight Curve" was drawn by subtracting from the animal's initial weight successive decrements calculated from the known loss of nitrogen. Deviations above this line of the curve of true body weight may be regarded as evidence of water retention. It is seen that some retention occurred early in the experiment even when the diet contained very little salt. Examination of the dog during this stage showed that the tissues of the groin and abdominal wall had become full although there was no palpable edema. The institution of high salt feeding was followed by a series of changing responses which are shown both by the weight curve and by the columns indicating the sodium balance—first a 3-day period of approximate salt equilibrium associated with a flat weight curve, second a 6-day period during which much salt was retained and the body weight increased 3 kilograms and massive edema appeared, and finally a 5-day period and a 12-day period during which the balance was negative and rapid loss of weight with subsidence of edema occurred. The experiment was terminated at this time because the animal's condition seemed critical. After a short period on a good ration she made an excellent recovery.

In this experiment, then, there have been reproduced both of the phenomena in which we are interested, namely, marked fluid retention resulting from the ingestion of salt, and spontaneous diuresis with loss of edema at a time when it might seem that the stage was set for further retention. By way of explanation it is suggested that a sudden increase in the quantity of ingested salt leads to an at least temporary increase in the volume of the blood. Such an increase implies some dilution of the plasma proteins and is possibly attended by a slight rise in capillary

blood pressure. Either of these changes would disturb the balance of forces so as to increase filtration from the capillaries and provide an increment in the mechanical stress to be borne by the tissues. There can be no doubt that the tissues of the healthy animal are able to withstand a stress of this magnitude. They may yield slightly and so permit a small increase in the total volume of interstitial fluid but edema does not result. In the animal with depleted plasma proteins, however, the increment of stress may be delivered at a time when the elastic strength of the tissues is near the yielding point. Even a small increment at this time could pass the limit of elastic strength, at which point the rapid accumulation of edema fluid would begin and go on until a stage was reached when the tissues were not able to hold more fluid. At this stage, or possibly even before, the renal mechanism responsible for diuresis may be called into action. In the experiment before us the curves for the plasma proteins suggest that diuresis caused a reduction in blood volume for we find that both albumin and globulin rose without change in their ratio. It is not possible to think of this rise as having resulted from actual protein regeneration. Now, the removal of fluid from the blood stream as well as from the tissues incriminates the kidney as being primarily responsible for the diuresis. For, if the motivating factor had been one which caused overloaded tissues to discharge their fluid we should not have expected the circulating blood to give up more than the extra amount of fluid received. In this case, then, the establishment of renal diuresis was sufficient to annul completely the tendency to fluid retention caused by the low serum proteins. The sequence of events involved may possibly have been as follows: (1) renal changes initiating diuresis, (2) decrease in the volume of the blood, (3) increase in the concentration of protein in the plasma, (4) a possible lowering of capillary blood pressure, and (5) discharge of fluid from the tissues into the blood stream.

The nature of the change in the kidney responsible for diuresis cannot concern us here. Indeed, it is far from established that renal change is either always or even most

often the cause of diuresis. On the contrary evidence exists which suggests that the process may sometimes be initiated by changes of an unknown nature in the tissues. And similarly it is possible that the steps involved in the retention of fluid which follows the administration of salt are not so simple as those which have been pictured. It is necessary, then, to confess much ignorance and having so confessed I trust you will not judge me harshly for having attempted to provide that which claims to be no more than an *understandable* basis for the phenomena.

To conclude and summarize: I have set before you this evening a list of factors which are concerned in fixing the distribution of fluid between the plasma and the interstitial spaces. Primary consideration has been given to those forces which control directly the movement of fluid across the capillary. The forces include the colloid osmotic pressure of the serum, the intracapillary blood pressure, the colloid osmotic pressure of tissue fluid, and mechanical pressure in the tissue spaces. During health the balance between the opposing forces is so beautifully adjusted that appreciable quantities of free fluid do not collect in the intercellular spaces. A change, however, in the direction which favors the filtration of fluid from the capillaries means an increment in the mechanical stress which the interstitial spaces must withstand and may lead to the development of edema. The existence of an effective osmotic force across the capillary is immediately dependent upon relative impermeability of its wall for protein. We have seen that edema may result from loss of this impermeability and that the loss may be due to allergic disease or to inflammation. Conversely, the degree of impermeability may be increased, and so provide a partial compensatory mechanism, in conditions in which the colloid osmotic pressure of plasma is abnormally low. We have further seen that the osmotic pressure of tissue fluid depends in large part upon the constancy with which protein is removed from the tissues via the lymphatics and that mechanical pressure in the intercellular spaces varies both with the activity of the lymphatics and with the elasticity of sur-

rounding tissue. I have pointed out that remote influences such as an excessive loss of protein in the urine or prolonged maintenance on a diet deficient in protein may lead to depletion of the serum proteins and therefore to a decrease in the effective osmotic pressure of plasma, that venous obstruction or venous stasis from myocardial failure may raise blood pressure within the capillaries, and finally have suggested that both forces on the inside of the wall of the capillary may be altered by changes within the kidney or by variations in the quantity of sodium chloride ingested.

CONGENITAL ANOMALIES OF METABOLISM WITH SPECIAL REFERENCE TO CYSTINURIA AND MYOPATHIES*

ERWIN BRAND

"Inborn errors of metabolism", has become a familiar term in medicine, since Garrod[1] first used it in his Croonian Lectures to designate a group of rare metabolic diseases, which he characterizes as follows: "Some of them are certainly, and all of them are probably, present from birth. The chemical error pursues an even course and shows no tendency to become aggravated as time goes on, and they are little likely to be influenced by any therapeutic measures at our disposal. Yet they are characterized by wide departures from the normal of the species far more conspicuous than any ordinary individual variations, and one is tempted to regard them as metabolic sports, the chemical analogues of structural malformations." Among these conditions, Garrod includes the following:

Albinism	Cystinuria
Pentosuria	Congenital Porphyrinuria and
Alkaptonuria	Congenital Steatorrhoea.

Because of the familial character of muscular dystrophy and the striking disturbance in creatine and creatinine metabolism observed in these patients, and because of the possibility that it may be metabolic in nature, we will consider this disease in the group of inborn errors of metabolism.

The limited time at one's disposal renders it unfeasible to discuss in any detail the various metabolic conditions which have been enumerated. It was thought, therefore, that it would be preferable to consider only a few of these diseases and I will restrict myself accordingly to cystinuria and myopathies.

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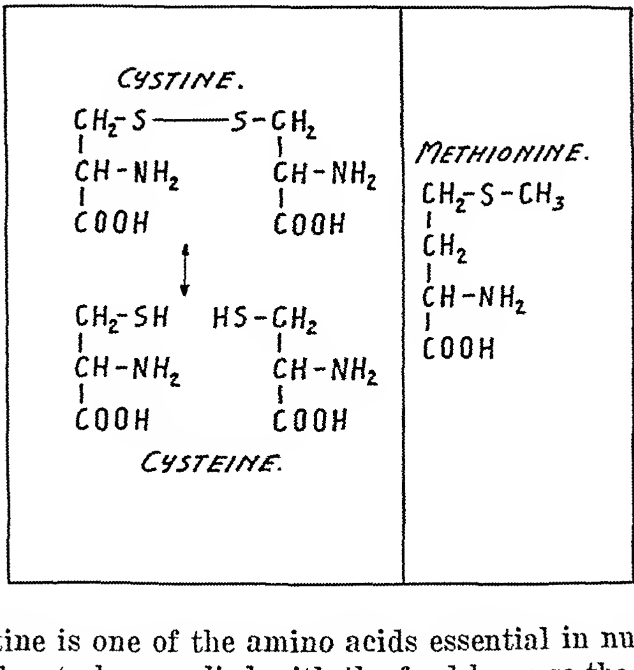
* Delivered October 27, 1933.

I. Cystinuria

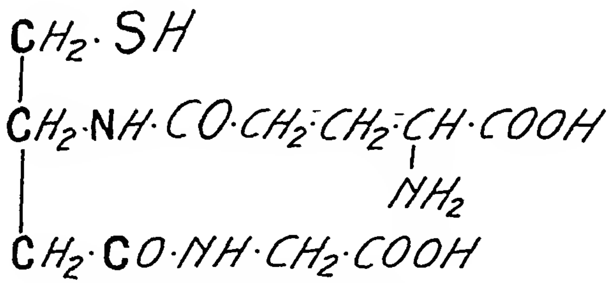
Cystine was discovered in 1810 by Wollaston, who isolated it from a urinary calculus. Almost 90 years elapsed before it was found that many proteins yielded this amino acid upon acid hydrolysis. Cystine contains sulfur in its molecule in the form of an SS or a disulfide linkage. Cystine can be reduced by various agents to two molecules of cysteine, which now contains an SH group. Cysteine on the other hand may be oxidized to cystine. Cystine remained for many years the only sulfur containing constituent of proteins. Only recently, another sulfur containing amino acid, methionine, was discovered.



Cystine is one of the amino acids essential in nutrition, *i.e.*, it has to be supplied with the food because the animal body is not able to synthesize it. Cystine or cystine derivatives occur in all tissues. Particularly large amounts are present in the keratinous tissues such as horn, nails, hair and epidermis.

Of great importance is the recent discovery of Sir Frederick Gowland Hopkins, that cysteine exists in all cells in the form of a tripeptide, glutathione. Three amino

acids, cysteine, glycine and glumatic acid, combine to form the glutathione molecule. Glutathione plays an important role in the oxidation and reduction mechanisms of most cells.



GLUTATHIONE

A brief analysis of our knowledge concerning normal sulfur metabolism seems advisable before entering into a discussion of its disturbance in cystinuria. A small portion of the sulfur is present in saliva and in gastric juice as thiocyanate and in the bile as taurine. Some sulfur occurs in the tissues, especially in liver and blood, as glutathione. Most of the sulfur, however, is found as a constituent of the proteins of food and tissues.

Only small amounts of sulfur are excreted in the alimentary canal and almost all of the sulfur of food and tissues is oxidized to sulfuric acid and excreted in the urine as inorganic sulfate. Part of these sulfates appears in the urine combined with certain aromatic or other constituents in the form of ethereal sulfates. The sum of the inorganic and ethereal sulfates is designated as total sulfates and makes up about 90 to 95 per cent of the total sulfur excreted in the urine. The rest consists of sulfur compounds like thiosulfate, thiocyanate and other organic sulfur compounds which are, as yet, not very well known. This fraction of the urinary sulfur is called neutral or organic sulfur and constitutes usually only about 5 per cent of the total urinary S.

PARTITION of URINARY SULFUR. (AVERAGE NORMAL DIET.)		
	TOTAL SULFATE %	NEUTRAL SULFUR %
NORMAL	95	5
CYSTINURIC (TYPICAL CASE)	55	45

In cystinuria, we have an excretion of cystine in the urine which excretion may amount to from ½ - 2 gms. daily. Cystine, being an organic sulfur compound, is determined as part of the neutral sulfur fraction of the urine. In a case of cystinuria we will, therefore, note a decided increase in the neutral sulfur fraction of the urine, which increase however is at the expense of the sulfate excretion, which is decreased. Thus the sulfates may amount to only 55 per cent instead of 90 per cent of the total sulfur, while the neutral sulfur may be as high as 40 p... cent or 50 per cent. The decrease of sulfate excretion ... at the expense of the inorganic sulfates, the ex... ethereal sulfates remains normal.

...ways excrete inorganic sulfates and only ...of the catabolized proteins is ...rror in metabolism, in Garrod's ... A possible explanation for this ...etabolic error may be found in ...iments which will be discussed

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titative methods for the determination of cystine in the urine. Among the latter the Folin test in its various modifications and the highly specific Sullivan reaction are worthy of mention.

Regarding the incidence of cystinuria it is interesting to note that up to 1916 we find only 107 cases of cystine calculi reported in the period of more than a century after Wollaston's original observation. Since then the number of cases of cystinuria reported has been large and H. B. Lewis[2] found at least 20 definite cases in an examination of about 11,000 urines of healthy young men and women.

The cystinuric loses appreciable amounts of cystine daily in the urine, apparently however without any ill effect. The only complication as far as one knows is the formation of cystine stones in the urinary tract, cystine being a very insoluble amino acid, its solubility in water being only 1 part in 10,000.

The cystine stones tend to form in the kidney pelvis, from which they may pass through the ureter into the bladder. The percentage of cases with stone formation is not as high as one would expect and some authors claim that only 3 per cent of cystinurics form stones. Cystine stones weighing as much as 50 gms. have been found, and they have been reported in children even as young as two years of age. It is not unusual that a kidney is completely blocked and destroyed by cystine stones.

In order to prevent or minimize stone formation in cystinuria a low protein diet and alkali administration have been frequently advocated. In this connection an observation by Dr. G. F. Cahill of the Squier Urological Clinic of the Presbyterian Hospital on a patient suffering from cystinuria with stone formation may be of interest. The right kidney of this patient was removed because it was completely destroyed by stones; X-ray examination showed no stones in the left kidney and ureter. The patient was then put on a low protein diet plus alkali. About three months following the removal of the right kidney a cystine

INCREASE of CYSTINE in CYSTINURIC URINE on STANDING.

URINE SPECIMEN	A			B		
AGE of SPECIMEN	3 hrs.	8 hrs.	24 hrs.	3 hrs.	8 hrs.	24 hrs.
CYSTINE (SULLIVAN) — mgs.	101	123	157	213	278	338
CYSTINE (SULLIVAN) — % of NEUTRAL S	43	53	67	59	76	92

stone was observed in the left ureter. Seventeen days later the stone had approximately doubled in size and had to be removed by surgical means. During this entire period the patient had been on a low protein diet plus alkali.

For a number of reasons, which time does not permit me to discuss, we believe that both a low protein diet and alkali administration are of questionable value in cystinuria. It is our opinion that cystinuric patients suffering from stone formation should receive in their diet a sufficient amount of protein to satisfy their demands for nitrogen and for the important essential amino acids including cystine. About 50-70 gms. of protein of good nutritional value should be given, depending on age and weight of the patient.

In regard to the form in which cystine may be excreted in cases of cystinuria it may be of interest to present an observation which was made a few years ago[3]. It was found with the aid of the Sullivan reaction, which is highly specific for cystine, that a fresh cystinuric urine yielded less cystine than the same urine after it had been standing for 24 hours.

This finding was interpreted as indicating that in cases of cystinuria there may be excreted not free cystine but a complex which decomposes in the urine with the liberation of free cystine. In regard to the nature of this compound

no information is available, but we are speculating now about the possibility that it may be a cysteine compound, containing perhaps an ether or thioxyester linkage.

On a standard diet cystinuric patients excrete daily fairly uniform amounts of cystine. An increase in the protein intake is followed by an increase in the cystine excretion and a decrease in the protein intake is followed by a decrease in the excretion of cystine. However, if free cystine is fed to a cystinuric, no additional cystine appears in the urine, and all of it is burned to sulfuric acid being excreted as such. It has been observed time and again that the cystinuric patient oxidizes free cystine to about the same extent as the normal person and excretes it as inorganic sulfate. Investigators have always been at a loss to explain how a cystinuric patient, on the one hand, can oxidize the free amino acid cystine when it is fed as such and on the other hand, cannot oxidize the same amino acid when it is given in combined form as protein.

Dr. Cahill, Dr. Harris and I had recently the opportunity to carry out a series of metabolic investigations on a cystinuric patient of the Squier Urological Clinic of the Presbyterian Hospital. The work was aided by grants from the Committee on Scientific Research of the American Medical Association[4].

In these experiments a cystinuric patient was kept for a period of approximately four months on a standard meat free diet and his urine analyzed daily for various nitrogenous and sulfur constituents. In addition the cystine sulfur was determined by both the Folin and the Sullivan methods.

During experimental periods of 3 days each the following compounds were fed in the quantities (equivalent amounts of sulfur) indicated: cystine (6.4 gms.), glutathione (16 gms.), cysteine HCl (8.8 gms., neutralized) and dl-methionine (8 gms.). The experiments were carried out in triplicate except the one with glutathione which was repeated only once.

The results may be summarized as follows:

Cystine experiments showed that 94 per cent of the extra sulfur was excreted as inorganic sulfate and that there was no rise in the excretion of cystine.

Glutathione experiments showed that 80 per cent of the extra sulfur was excreted as inorganic sulfate and that there was a slight rise in the excretion of cystine which amounted to 9 per cent of the extra sulfur.

Cysteine experiments showed that only 34 per cent of the extra sulfur was excreted as inorganic sulfate while there was a large increase in the excretion of cystine, continuing for several days after the feeding, which increase in cystine excretion accounted for 66 per cent of the extra sulfur. The analyses also indicated that additional cystine and not cysteine was being excreted.

dl-Methionine experiments showed that only 34 per cent of the extra sulfur was excreted as inorganic sulfate while there was a large increase in the excretion of cystine continuing for several days after the feeding, which increase in cystine excretion amounted to 47 per cent of the extra sulfur; there was also a definite increase in the excretion of undetermined (non-cystine) neutral sulfur which amounted to 19 per cent of the extra sulfur. The analyses again indicated that additional cystine and not cysteine was being excreted.

These experiments tend to show that the metabolism of cystine may be quite different from that of cysteine and that these two compounds are not as interchangeable in intermediary metabolism as has been assumed generally. They further show that the metabolic behavior of an amino .id may vary markedly depending upon whether it is catabolized as a free amino acid (cysteine) or in combined form as a peptide (glutathione). The experiments also indicate that methionine may be metabolized via cysteine. Experiments by Jackson and Block[5] and by White and Lewis[6] have recently established a close metabolic interrelationship between methionine and cystine.

The above mentioned authors are inclined to interpret their findings as indicating that methionine may spare cystine. Our experiments however establish the possibility that in intermediary metabolism methionine, under conditions, may be transformed directly or indirectly into cystine via cysteine.

The finding that cystine is excreted following the administration of cysteine indicates the possible role of the kidney in the oxidation reduction mechanism of the SS-SH system.

It appears that the cystine which the cystinuric excretes in the urine may be derived, in part or in whole, from that portion of the protein sulfur which is present in the protein molecule in the form of methionine. Further experiments will be necessary to determine to what an extent cystinuria is primarily a disturbance in methionine metabolism.

The possibility of a disturbance in glutathione synthesis in cystinuria should be considered. This view would be in keeping with the aspects of intermediary protein metabolism indicated in a previous publication[7].

II. Myopathies

Although general attention has been directed to the myopathies since Aran's communication published in 1850 and much has been written regarding them, our insight into the pathogenesis of this group of diseases has remained rather superficial and controversial. The concept of the myopathies is as yet not firmly established and the characteristics of the various groups are not clearly delineated, nor their dividing lines sharply drawn.

In an editorial discussion[8] on the muscular dystrophies in the Lancet in 1925, it was pointed out that one is not likely to reach any rational conception of treatment of the myopathies from clinical studies alone, and that chemical investigation in these conditions is an uncultivated field which will repay any labor that is spent on it.

It was shown by Folin[9] in 1905 and a little later by Klercker[10] that the normal adult excretes from day to day uniform amounts of creatinine in the urine but no creatine or only very small amounts, especially in the case of the female. It was also shown that these findings are not readily altered in the normal person by the level of the protein in the diet. It has been claimed that the amount of creatinine excreted bears some relation to muscular mass but not to the tone or activity of the muscles. The significance of this relationship is as yet not entirely clear. Although some believe that creatinine is related to the amount of creatine or creatine phosphoric acid stored in the muscles, the origin of creatinine from this source is by no means established, nor is the mechanism of its formation known[11]. There appears to be, however, an intimate relation to carbohydrate metabolism.

The relative amount of creatine in the urine is materially increased during childhood up to between 10 and 15 years of age and also in the adult during certain physiologic processes such as lactation or in a variety of pathologic processes such as fever, starvation, severe diabetes or other conditions associated with deprivation of carbohydrates, severe exophthalmic goiter and certain myopathies.

Rosenthal[12] knew as early as 1870 that certain myopathies were associated with a disturbance in creatinine excretion as indicated by a diminished daily output. This observation was confirmed by various investigators and particularly by Spriggs[13] using the improved Folin method for creatinine determination.

P. A. Levene and Kristeller[14], in 1909, working in Montefiore Hospital, carried out quantitative studies on the urine of patients with various muscular disturbances and ound that in cases of progressive muscular dystrophy there was not only a low creatinine but also a high creatine output. They further observed that increased amounts of protein in the diet increased the amount of creatine excreted by such patients. And unlike normal adults, these persons also eliminated a large percentage of small

amounts of creatine administered orally. (Such diminished tolerance to creatine is present in other types of creatinuria, and when present may be influenced by the level of the protein intake.)

Gibson and Martin[15] (1922) tried to determine what constituent of the protein molecule produced the rise in creatine excretion in muscular dystrophy but without any success.

Early in 1928 Dr. M. Sandberg and I in the laboratory division of Montefiore Hospital under Dr. David Marine started to cooperate with Dr. M. M. Harris of the Medical Service of Dr. B. S. Oppenheimer on an extensive metabolic investigation on the creatine and creatinine metabolism of patients with muscular dystrophy. The work was continued later by Dr. Harris and myself at the New York State Psychiatric Institute and Hospital.

The patients were kept under standardized conditions over a prolonged period of time and their urine analyzed daily for creatine, creatinine and other constituents. The effect of oral administration of various substances which were superimposed on the diet was studied.

It was found[16] on repeated experiments that glycine produced an appreciable increase in the creatine excretion in these patients. Arginine, cystine, glutamic acid, histidine, nucleic acid and various other compounds had no such effect.

It is well known that the administration of benzoic acid results in a loss of glycine from the body, owing to the excretion of a combination of the benzoic acid with the glycine in the form of hippuric acid. This fact was utilized to determine the effect of such losses of glycine on the creatine excretion in our cases. It was repeatedly found that the administration of benzoic acid produced a prompt and appreciable decrease in the creatinuria[16].

The following is a list of the compounds investigated.

COMPOUNDS STUDIED IN MUSCULAR DYSTROPHY

Glycine	Urea
Guanido acetic acid	Uric acid
Sarcosine	Creatinine
i-Alanine	Creatine
d-Glutamic acid	Isocreatine
d-Arginine	Betaine
l-Histidine	Nucleic acid
l-Cystine	Edestin
Cysteine	Gelatin
i-Serine	Casein
l-Tyrosine	Ammonium acetate
d-Arginine and glycine	Ammonium chloride
Glycine and d-Glutamic acid	Benzoic acid
Glycine and l-Cystine	Phenylacetic acid
Glycine, d-Glutamic acid and l- Cystine	Ephedrine
Glycyl-Glycine	
Glucose	
Lactic acid	

Since, as already stated, the feeding of glutamic acid produced no effect on the creatinuria, it was considered desirable to investigate what effect the withdrawal of glutamic acid would have on the creatine excretion. This was accomplished by feeding phenylacetic acid, which, in man, is known to be excreted in combination with glutamine as phenylacetylglutamine. It was found[7,17] that such feeding had no effect on the level of creatine excretion.

We are inclined to infer from these 5 experiments that the feeding of brombenzene which removes cysteine from the metabolic mixture would be without effect on creatine excretion, since cystine did not give a rise in creatine excretion. Brombenzene is probably rather toxic so that we have not carried out such experiments on patients.

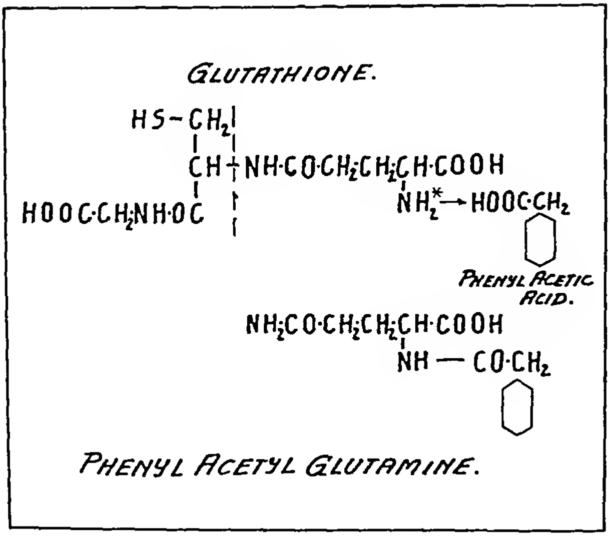
We have been led to believe from our experiments[7,17] that glycine, glutamic acid and cystine are probably present

in the metabolic mixture, although not as free amino acids as tissue analyses indicate, but in some combined form. In glutathione which is present in the body in large amounts we have such a combination. Now it is an interesting fact as Waelsch[18] and also Power[19] have pointed out, that the three amino acids—glycine, glutamic acid and cysteine which are the only three amino acids known to play a role in processes of detoxification are exactly those one finds in the molecule of glutathione.

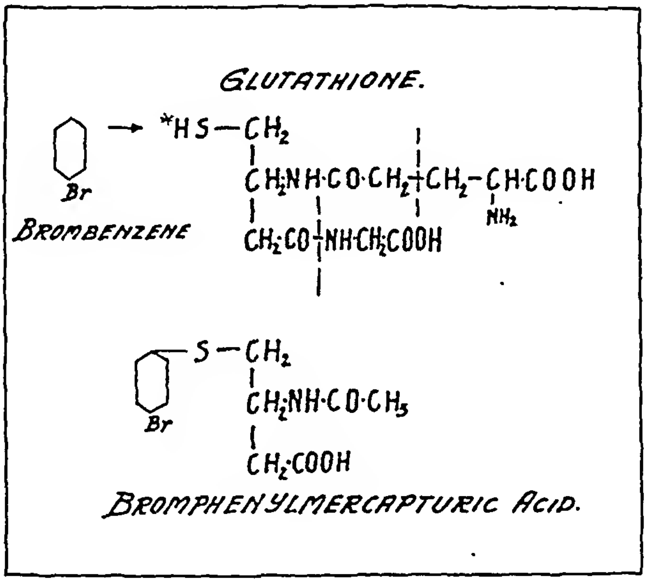
Since the feeding of benzoic acid markedly reduces creatine excretion in the cases of muscular dystrophy and if the glycine used to detoxify this substance comes from glutathione, then it would appear very possible that glycine plays its role in creatine metabolism via glutathione.

It may be interesting at this point to indicate the possible manner in which glutathione detoxifies phenylacetic acid and brombenzene.

E.g., phenylacetic acid would combine with α-amino group of the glutamic acid radical of glutathione (indicated by * in the formula), following which the side chain splits off completely at the α-carbon of the cysteine liberating phenylacetylglutamine.



Brombenzene would combine with the SH group of glutathione (indicated by * in the formula), following which the glycine is split off and *B*-oxidation takes place on the center carbon atom of the glutamic acid radical. Thus the acetyl group of bromphenyl mercapturic acid would be a remnant of the glutamic acid radical of glutathione and not due to a special process of acetylation. It is interesting to note that glutathione in this way may yield, under conditions, two molecules of glycine[16].



In 1929 we had occasion to discuss some phases of our studies with Professor Karl Thomas at the International Physiological Congress in Boston and to show him our detailed protocols when he visited us in New York City following the meeting. On his return to Leipzig, he repeated some of his earlier experiments on the origin of creatine with his special compounds on patients with muscular dystrophy but with negative results.

However, on repeating the experiments with glycine he was glad to be able to confirm our findings. Because of this established relation of glycine to creatine he undertook the

problem of the possible therapeutic effect of glycine in muscular dystrophy from its prolonged oral administration. Thomas, Milhorat and Techner[20] reported that some patients with muscular dystrophy were markedly improved from such therapy.

In this connection, it may be of interest to point out that only one or two out of 11 cases of muscular dystrophy reported by Milhorat with case histories showed definite improvement upon glycine administration. It is worthy of note that in these two cases, before the experiment was started, the average daily excretion of creatine was only 0.02 and 0.03 gm. respectively on a creatine-free diet. Considering the fact that in these cases the disease had been present for 14 and 15 years and that it was associated with appreciable physical disabilities, the almost negligible degree of creatinuria would seem most unusual for progressive muscular dystrophy. This would lead one to suspect that the cases perhaps belong to a special clinical group which responds to glycine treatment.

In 1932, we extended our metabolic studies in the myopathies to the investigation of the therapeutic effects claimed to have been obtained from prolonged administration of glycine. This phase of the work [17, 21] was carried out at the Psychiatric Institute with the cooperation of the Research Committee of the Neurological Institute and especially that of Drs. E. G. Zabriskie and C. C. Hare, who gave us valuable opinions regarding the neurological status of the cases. The work was aided, in part, by a grant from the Chemical Foundation. Up to date we have carried out metabolic and therapeutic observations in 46 cases of progressive muscular dystrophy of various types and severity and in 24 cases of various neuromuscular conditions and also several cases of myasthenia gravis and Graves disease. None of our patients with muscular dystrophy, receiving glycine therapy have shown any striking improvement such as that reported by Thomas, Milhorat and Techner and by Kostakoff and Slauck[22].

Of course it would be difficult to ascertain whether any slight improvement had occurred which could not be readily detected owing to the lack of satisfactory methods for measuring such improvement. In a number of cases, the families were of the opinion that the children were more active as a result of the therapy. However, objectively, no notable change has been observed as yet. Some of the patients have been receiving glycine for a period of more than one year and with perhaps one exception, there has been no apparent marked progress of the disease. One case of muscular dystrophy in a male of 45 years of age, who has been receiving glycine and glycine plus ephedrine for about one year, reported that he feels stronger and measurement of his muscles indicated that there has probably been an increase in the size of the musculature around one of the shoulders, which he felt was definitely stronger.

Boothby[23] of the Mayo Clinic, feels that glycine increases the efficacy of ephedrine in the treatment of myasthenia gravis. From our small experience with such cases, we can confirm the efficacy of ephedrine in some of the patients. We are not ready, however, to express any opinion regarding the effect of glycine. The experience of Boothby[23] and Moersch[24] regarding the effect of glycine in muscular dystrophy, as expressed at the last meeting of the American Medical Association, is essentially similar to our own.

The administration of glycine in a larger group of cases of muscular dystrophy is being continued particularly in children at an early stage of the disease in an endeavor to determine the possible therapeutic effect of glycine on the course of the disease over a period of years. Such continued and prolonged studies are made necessary because of the usual slow progress of the disease. Therapy also along other lines is being investigated.

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GOUT*

Leopold Lichtwitz

A physician, fifty years of age, "with a large head, of a full, humid and lax habitus, of a luxurious and vigorous constitution with excellent vital stamina," as Sydenham portrayed him, or in the words of Garrod, a man "of robust and large body, large head, of a full and corpulent habitus, whose skin is covered with a thick rete mucosum,"—a man, as Cullen described him, "of choleric-sanguine temperament," or as Gairdner stated, "of great vigor and apparent health,"—a physician devoted to science and with a warm heart for his patients, full of the love of life, humanity, art, and progress, gifted with a sense of humor, returns home on a winter evening, from a gay dinner with his friends. *Getting out of his car his right foot touches the* ground and he feels an overpowering pain in the basal joint of the great toe. He is unable to walk. A sweat breaks out. He removes his hat to dry his forehead, revealing thick shaggy eyebrows and a full crown of wavy hair. A few minutes later the pain is gone and believing that he had made a misstep, he forgets the incident entirely. The doctor goes to bed, and as usual, quickly falls asleep. About two hours later, between one and two o'clock, he awakens with a terrible pain in the same joint. At once he examines the painful foot. He notices no redness or swelling but finds the cutaneous veins of the foot and leg strikingly full and tense. The doctor faces his first gouty attack, so incomparably described from personal experience by that Hippocrates of English medicine, Sydenham. I shall not repeat Sydenham's description. His treatise is a delight and belongs to those classics which form the background of medical education.

Every detail of the short story just related is typical and has been repeated countless times during the course of centuries. Age, somatic and psychic constitution, season

*Delivered October 27, 1933.

and circumstance are characteristic for the gouty diathesis and the gouty attack. This first attack establishes the existence of a chronic disease. For, actually, gout is always a chronic disease although the stage characterized by the explosive attack is generally called acute gout. The predisposition to attacks and other manifestations is, indeed, latent but ever present.

This first attack was precipitated by extraneous and accidental circumstances such as cold weather, a good dinner and wine. In the absence of these factors the attack would not have occurred on this particular night and perhaps never. Obviously internal conditions were ripe for and conducive to an attack. In other words, the doctor, even before the acute episode, was already gouty. We must ask, "Is there any possibility of recognizing gout before the attack?"

This question brings up the difficult matter of the gouty constitution and of latent gout. Widely divergent views exist. There are those who frequently make a diagnosis of gout and use the term in a very broad sense. On the other hand, there are others who go so far as to deny the existence of the disease. Osler found that gout was often unrecognized in this country and Pratt has drawn particular attention to the scepticism in the minds of many practitioners regarding the existence of the disease. At the present time the recognition of gout in latent or atypical form is little recognized. In Germany, France, America, and even in England—the home of gout—the number of those afflicted with the typical disease is constantly decreasing. That its incidence was decreasing was observed as early as 1881 by Charcot.

The waves in the frequency and character of diseases constitute a curious phenomenon. In gout this is especially striking. Personality and character color the gouty picture in a remarkable way. No disease has such a predilection for eminent men. Among those in our own profession—to name only a few—are Sydenham, Harvey,

Linné, Widal. Amongst the men in pure science are Leibnitz and Newton, and among the historical figures are found such men as Wallenstein, Condé, Fox, the two Pitts, and many others. Charcot said, "the most distinguished statesmen become victims of gout." This situation seems to be much changed. The type of person has changed. The pyknics have lost in numbers and more so in influence. In place of the straightforward, erect, unaffected, humorous and generally rather asthenic type we find the high strung, rather nervous, and essentially asthenic type of diplomat whose bodily and mental makeup has not the characteristics of the typical gouty constitution. One can see that the fate of mankind is close to the history of gout. Gairdner, having the two Pitts in mind, stated that the disease is sometimes a matter of national and imperial interest.

The relation of the clinical picture of gout to personality is more marked than in any other disease. In the words of Gairdner, "The minute features of gout are found as various as the individuals whom it assails. We hear the patient speak of "his" or "my" gout, as if they were things of quite distinct creation."

In the presence of the constitution described, gout becomes manifest in persons who eat and drink excessively, at 50 to 60 years of age, when bodily exercise is reduced. In a smaller number of cases gout occurs in the absence of evidence of this constitution and in spite of physical activity and moderation in habits.

The importance of moderation and exercise in relation to etiology, prophylaxis and therapy of gout was recognized by Hippocrates. In the older literature there are interesting examples given (Schenkins, Gairdner) of rich men living in luxury, ease and indulgence, who, on becoming poor, were freed from their gout because of a sparing diet and bodily exercise or laborious occupation. Even many and large chalkstones (tophi) covering the joints disappeared.

These simple factors, capable of so much influencing gout in a marked form, may certainly be expected to be still more significant in prophylaxis. But there will be no progress and accomplishment if we are unable to recognize the gouty constitution as well as the forerunners of the gouty attack, and can convince the future victims of the necessity of prophylaxis.

Some facts concerning this disease are made clear when we realize that heredity plays a greater role in this disease than in any other except migraine. An hereditary factor is at play in at least 50 per cent of the cases. According to William Roberts, 75 per cent come of gouty stock. In a case cited by Garrod and in one of my own cases, gout could be traced in the family as far back as 400 years. The stronger the hereditary factor the earlier in life does the disease become manifest. This is especially true, it seems, if gout is inherited from the mother. Rarely, however, does the disease begin in childhood or before the age of twenty. Women are much less frequently affected by gout, the ratio to men being 1:7.

When investigating the constitutional and hereditary factors, the inquiry should not be limited to gout. In the family as well as in the personal histories of the gouty, very frequently are discovered migraine and various manifestations of the angiospastic diathesis: also asthma, spasmodic vomiting, urticaria, acute articular rheumatism, and arthritis without urate deposits. The fact that an individual may in youth suffer from acute articular rheumatism and later in life develop gout, was pointed out by Llewellyn. Recamier said, "Gout and migraine are sisters." When migraine disappears, gout appears. The latter fact is well illustrated by a remarkable case cited by Trousseau. It is also well known that asthma may alternate with gout and that a prolonged attack of gout may be terminated with the outbreak of an urticarial rash. Duckworth made the significant observation that daughters of gouty fathers frequently suffer from so-called chronic rheumatic arthritis. This association of gout with

other diseases has been overlooked by physicians because of the overestimation of the significance of uric acid.

The association of gout with other diseases is the basis of the French concept of "arthritism," which has resulted in the recognition of gout as a member of the great family of allergic diseases. The joints and especially the periarticular tissues are known to be sites of marked allergic sensitiveness. It is not surprising, therefore, that Heberden's nodules frequently develop in individuals predisposed to gout, migraine and asthma, and in daughters of gouty fathers (Lécorchè).

The older literature contains examples of gouty fits occurring after certain foods. It has also been known for a long time that a specific hypersensitiveness may exist for a certain alcoholic beverage, and thus give rise to attacks of gout. One person may have an idiosyncrasy to beer, another to champagne. Widal who was gouty himself and was the first to recognize the allergic nature of gout, noted a hypersensitiveness to a particular wine and came to the conclusion that the allergen was a protein substance formed from the yeast.

In gout as in all other conditions in which allergy plays a role, hypersensitiveness is not limited specifically to a single substance. It exists not only for exogenic substances such as those that are introduced with the food, but also for a number of substances which are developed in the body itself. Active substances of the latter type are formed in the tissues by mild or severe tissue damage, by contusions, operative manipulations, etc. They also develop under the influence of local cooling, as, for example, in cold, wet feet, and as a result of emotional disturbances and strenuous mental effort. All these factors play a role in the manifestations of gout and in determining the occurrence of the gouty attack. Thus Garrod remarked that a blow, a fall or injury frequently determines the localization of the attack. A letter from Sydenham to Dr. Short is illustrative of the influence of emotions and mental strain. In it Sydenham says, "By applying my mind to its

utmost and by bringing all my powers of thought on the subject (namely the subject gout) I brought on a fit of gout as I had never suffered from. Whenever I returned to my studies, gout returned to me." It is evident then, that gout is not only, as the older physicians asserted, a daughter of Venus and Bacchus, but that Pallas Athena has some part in the child.

Simulating other allergic diseases, the gouty attack, at least in a certain stage of the disease, occurs periodically, at regular intervals. As after other allergic attacks there is also following a gouty one, a period of well being. "The worse the pain, the shorter the fit; the shorter the fit the longer and more complete the intermission." (Sydenham). The attack seems to be in the nature of a purifying thunderstorm. It is in all probability correct to say that the attack results in desensitization.

Besides its connection with allergic disease gout is related to the formation of nephrolithiasis. Garrod wrote, "In later years gout develops when in early life gravel and calculi are formed." This opinion finds no corroboration in our time since kidney stones are so frequent and typical gout so uncommon. Unquestionably gout leads to the formation of stones in some instances and, indeed, not only urate but also oxalate stones.

The kidney in the gouty diathesis is inclined to the formation of urinary sediment. We are dealing with a kidney secretion of inferior value, demonstrating in itself the participation of the kidney in this diathesis. In gout as in the new born there are formed uric acid infarcts in the form of whitish streaks in the medullary substance, sometimes in the pyramids. This deposition of urates in the parenchyma as well as the formation of gravel and stones may be the cause of the hematuria which we frequently encounter in the gouty. This relation of renal calculi to gout led Erasmus to express himself in a letter to Thomas Moore, thus, "Thou hast gravel and I have gout. We have married two sisters."

Having investigated the constitutional and hereditary situation and having been either led to suspect or actually recognize a gouty predisposition in an individual, the question arises: Is there from this point until the first attack a completely uneventful hiatus, or are there symptoms, or signals, perhaps slightly noticeable, which give the clue to the experienced clinician? The answer is: Yes, there are prodromal symptoms which although in no way specific are significant because they are numerous.

The forerunners of the attack at first involve the organs of digestion. Dyspepsia, capricious appetite, gastric acidity, pyrosis, constipation, and attacks of sudden painful diarrhea, mostly at night, occur. The tongue is heavily coated, red at the tip and edges, and there is a disagreeable taste in the mouth. After meals there is a feeling of distension in the epigastrium, a fullness over the hepatic region and a slight swelling of the liver. Enlargement of the liver occurs normally during the hours of digestion but not to the degree to which it does in this stage of developing gout. This enlargement is the result of contraction of the hepatic veins. We know that this contracting apparatus is subject to allergic sensitivity and shows its greatest reaction in anaphylactic shock. It is therefore permissible to presume that allergic sensitivity plays a role in the enlargement of the liver in gout.

Another prodromal symptom is the reduction of urinary output, occurring from time to time, not noticeable most of the time, yet occasionally expressing itself as visible swelling of the hands. A tendency to edema, and edema proper, may be of allergic origin. There are other cutaneous manifestations. Gairdner notes that an unnatural dryness of the skin may precede the attack by months and even years. Sweat and sebaceous exudation of the armpits and toes disappear. These parts become hot and itching. The most common conditions are urticaria, psoriasis, eczema, especially dry eczema of the eyebrows. Pains in muscles and joints appear as abrupt twinges. Great tenderness of the feet develops while walk-

ing but may also occur while the patient is at rest or is lying in bed. The gouty may complain of tenderness, stiffness and a feeling of shortness in the tendo Achilles. Graves has emphasized the occurrence of sudden pains or twitches which last only for a few minutes or even seconds. Gairdner speaks of "a dull pain in the left side of the chest, pain, pricking and tenderness in the ears or at the side of the finger joints, pain in the eyeballs or in the lumbar regions and sciatica." He also draws attention to cramps of the muscles occurring at night or when walking.

The older physicians spoke of asthma, coughing, heartburn, oppression, and irregularities of the heart as forerunners of the attack. Today we are more reserved in the evaluation of these symptoms. We are, however, definitely certain of changes in the character and disposition as being forerunners of manifest gout. Lassitude, prostration, sleeping after food, interrupted sleep at night, are such symptoms. The person becomes hypochondriacal, morose, irritable and unable to perform any kind of intellectual labor. There are explosive mental outbursts. The irrascibility of the gouty is proverbial.

These symptoms are not of themselves characteristic. Yet they belong to gout. This is verified by the common observation that symptoms peculiar to the individual precede each attack for many years and that the patient who has not forgotten his first attack together with its prodromata can sense the approach of the next. His family and associates who have put up with this change in character and manners can similarly predict the visit of an attack.

It is the prodromal period which is the best time for treatment. But because of his confidence in his vitality and vigor, his unconscious conviction of his right to invulnerable health, both inherent in the very character of the gouty man, this causes him in most cases to neglect and suffer the forerunning symptoms and to refuse the advice of his wife and physician. The painful experiences of even many attacks will often not suffice to convince a

gouty person to change his mode of life. Thus the incurability of gout and its tendency to progress have their foundation in the gouty constitution proper.

Before an attack the prodromal symptoms increase but sometimes disappear to give way to an abnormal sense of well being which is in turn abruptly terminated by the attack.

Gout appears in various forms. We have spoken of acute and chronic gout. The terms regular, irregular, atonic and visceral gout have been in use for a long time. The older clinicians designated as retrocedent gout those diseases of the internal organs which made their appearance during an attack or at its sudden termination. Cerebral apoplexy and cardiac disturbances, when they occurred in an individual afflicted with gout, were labeled gouty.

The form in which gout appears is dependent upon the individual constitution. The manner in which gout changes in the course of years depends upon the changes in the individual brought about by the illness and advancing years.

The most satisfactory bird's eye view of the disease is given by Gairdner who divides the disease into three stages.

1. Attacks at regular or irregular and distant intervals. Unhurt constitution. Severe fits, but afterwards the patient feels little inconvenience and forgets his misfortune.

2. The fits are seldom as painful as in its earlier period, but frequent. Diminished strength. The step has lost its elasticity, the head its firmness and resolution, the handwriting becomes tremulous and indistinct. Any excess makes inconvenience (dyspepsia). Enlarged subcutaneous veins appear over the face. The eyes become bleared. Conjunctivae become filled with blood. The patient represents an altered being.

3. Melancholy stage. Rarely decided attack, but the malady is never absent. In summer there is a short intermission of suffering. Indigestion, muscular and nervous weakness, heart trouble.

Not every patient passes through these three stages. If gout affects an individual who does not possess the gouty constitution but is of asthenic type with muscular weakness and of a nervous temperament, the disease will express itself as atonic or irregular gout in the third stage.

The most certain of the diagnostic criteria of gout is the tophus. Tophi may appear before the first attack and are especially easy to recognize when situated at the margin of the ear (helix). They develop painlessly and are usually unnoticed. In its first stage the tophus is neither hard nor white but soft and apparently fluid in consistency. The skin covering it is unchanged. It is important to point out that the tophus does not develop as the result of inflammation. It gains its characteristic shape by filling with crystalline urate and by the thinning of the overlying skin. The formation and disappearance of tophi is independent of the occurrence of attacks. They are not tender—they do not show urates in every case, but always necrosis of tissue. According to the view of Ebstein, which I consider to be the correct one, though it be contrary to that of most pathologists, the tissue damage which ultimately leads to necrosis is the primary process. This tissue injury is not caused by the uric acid for the latter is not a toxin and is incapable of injuring tissues, as a study of uric acid infarcts in the new born readily discloses.

Since the time of Garrod the view that uric acid is a poison and is the toxin of gout has been firmly rooted in the minds of most physicians. There is no evidence for this view. Birds and reptiles form great quantities of uric acid from urea. It would be contrary to the wisdom of nature to form a toxic substance from a non-toxic one such as urea.

In gout uric acid is apparently retained in the body. This is attested to by the fact that hyperuricemia is demonstrable not always but in the majority of instances. Garrod was the first to suggest that a damage to the kidney was responsible for this retention. Later on this damage was expressed as a disturbance in the partial function of concentration of urate (Lichtwitz, Thannhauser) as it occurs in renal disease. Thus some patients with diseased kidneys show hyperuricemia and urate deposits but fail to give any evidence of gout.

Hyperuricemia and the gouty attack have no recognizable relationship. This is supported by many examples. I refer only to a few.

A very prominent physician who had previously suffered from severe attacks of gout is now free of them though his blood uric acid is 16 mgm: per cent. A patient at the Montefiore Hospital, gouty, with a tophus in his ear, has been free of attacks for a long time although his blood uric acid has ranged between 9.2 to 14.8 mgm. per cent. We have recently observed a 54 year old man with gout and calculi in his kidney, and saw him in typical colics with a blood urate of 6-7 mgm. per cent. Several weeks after an attack the patient became anuric as a result of ureteral obstruction by a calculus. His uricemia rose to 24 mgm. per cent but no attack occurred. On the other hand, it is well known that attacks may occur in the presence of a normal and even a subnormal uric acid content of the blood.

Sometimes tophi break through the skin, and chalk-like masses are evacuated which contain numerous crystalline needles of sodium biurate (Demonstration). It seems very peculiar that these skin wounds never become infected.

As mentioned above the first visible change in a gouty attack is local venous stasis, a phenomenon described by the older clinicians and noted in every instance by myself. Later the swelling appears and with its appearance the pain decreases. It seems, corresponding to Gairdner's

suggestion, that the attack begins with a peculiar local disturbance of the circulation affecting veins and capillaries. This may be the basis for the occurrence of gouty phlebitis as first described by Sir James Paget, and of ecchymosis in the skin covering the diseased joint.

In 70 per cent of the cases the first attack involves the basal joint of the great toe, which is exposed to the largest load and greatest pressure. A part which had previously been injured is certain to be the seat of the gouty inflammation in subsequent attacks.

In serious cases the disease is widespread, involving many joints, the muscles, cartilages, tendons and internal organs. In such cases one finds tophi in the cartilages of the nose, in the eyelids, auditory ossicles (Harvey), corpora cavernosa (priapism), atheromatous aorta and in the walls of the bronchi. Finally, in the words of Sydenham, "the whole body is converted into a tophus."

Many of the details of the gouty picture such as the ocular affections, the urethritis, the bone and joint destruction with its anatomic and roentgenographic features, and many others, cannot be considered tonight.

We come, finally, to a consideration of therapy.

Today, as in the time of Hippocrates, moderation and exercise are the most important factors in treatment.

Concerning dietary therapy one may say that the purine free diet stands much higher in the estimation of physicians than of the patients suffering from gout, and I might add, that their judgment deserves more consideration than that of other patients. Llewellyn makes the pointed remark, "The purine free diet smacks too much of the laboratory." It should only be ordered as a cure of limited duration for 4 to 6 weeks in the form of a raw food diet or as a grapecure. The individuality of the patient must be taken into consideration. A muscular and plethoric young man cannot be given the same diet as a weak old person with atonic gout. Limitation of food to a maintenance

level is much more important than elimination of the purine containing foods. Ebstein states that the gouty who have grown old in spite of their disease are almost always those who have been able to avoid obesity. Diet in general should be suited to the individual and the disease. Its preparation should be as simple as possible. A diet with limitation to one dish of meat or fish per day given only on 5 or 6 days per week is sufficient curtailment and is followed more rigorously by patients than the purine free diet. There is no need for the general prohibition of alcoholic beverages. I agree with Llewellyn that total abstinence is not prudent in middle or late life. Total abstainers are not exempt from gout. Which drinks are to be permitted depends upon the allergic sensitiveness *of the individual. The latter information can usually* be obtained from a study of the history.

During the attack rest is prescribed. Local applications, warm or cold, according to the patient's desire, should be applied. Cinchophen may be given in doses of 3 grams per day but for not longer than four successive days. This should be given together with a large amount of water or tea. Sodium salicylate 3-6 grams per day, if necessary by enema, is less harmful and nearly equally efficient.

The only specific against the gouty attack is colchicum. It should never be given, however, at the beginning of an attack and never to weakened individuals. Colchicum is in bad repute among many of the gouty, the reason being that when administered in high doses, as not infrequently happens there may ensue diarrhea, weakness and collapse. Gairdner in his remarks on therapy says, "Colchicum never more effectually relieves the patient than when it acts silently and peacefully, without producing any evacuation whatever or in any way disturbing the patient's comfort and ease." Experienced gouty patients advise that colchicum is best taken in the morning hours in ½ mgm. doses, three or four times during the first day, doubling the dose on the succeeding two or three days. It is re-

duced in quantity or entirely stopped when diarrhea appears or any other disturbance is manifested.

Colchicum exercises its pharmacologic effect on the capillaries and periarticular tissues, being capable in high dosage of causing arthritic attacks. This is of significance and is in harmony with the viewpoint that the gouty attack is an allergic reaction involving veins, capillaries and joints.

Nothing can be more unwise for the patient, than immediately after a cure of gout by this means to revert to the usual course of life. In the period after and between attacks the regulation of the mode of life is of prime importance. During this time, I believe, it is useful to put the patient on lemons and administer ½ to 1 teaspoonful of washed sulphur in water at night.

Sydenham concludes his famous dissertation on gout as follows: "As for a radical cure, this lies like Truth, at the bottom of a well; and so deep is it in the innermost recess of Nature that I know not when or by whom it will be brought forward into the light of day." These words still ring true today.

LIBRARY HOURS DURING THE SUMMER

As usual, the Library will be closed daily at 5 P. M. instead of 10:30 P. M., Wednesdays excepted, from June 15th to September 15th, inclusive. It will be open only on Wednesday evenings until 10:30 P. M.

THE LINSLY R. WILLIAMS MEMORIAL MEETING

To do honor to his memory, Fellows of the Academy and friends of Dr. Linsly R. Williams, gathered in Hosack Hall on April 26, 1934, to participate in a memorial meeting.

Dr. Bernard Sachs opened the meeting, and both as President of the Academy and as a devoted friend to Dr. Williams, pointed to the gathering as evidence of the deep affection in which he was held and the loss which was felt by the Fellowship of the Academy in the death of its first Director.

The program of the meeting included three addresses dealing with various aspects of Dr. Williams' life.

Dr. John H. Finley spoke on Dr. Williams as a Citizen. With the text taken from the Religio Medici of Sir Thomas Browne, "There is a nobility without heraldry, natural dignity, whereby one man is ranked with another, another filed before him, according to the quality of his desert and preeminence of his good parts," Dr. Finley dwelt upon the person and services of Dr. Williams. "His head ever moved a little before his square shoulders as if ever inquiring the way of advance and ready for anything. But seeing his eyes, one could never mistake him for another — the gentleness of their salutation, the depth of understanding which they revealed, the quiet determination and their preparation against any surprise . . . Linsly Williams died *a man*, who lived up to its high definition — a man 'beloved and elect of men.' "

Dr. Livingston Farrand dealt with Dr. Williams' Contribution to Public Health and Medicine, beginning with Dr. Williams' entrance upon the practice of medicine in [illegible] York [illegible]d his participation in the Metropolitan [illegible]ssion organized in 1908. The subsequent [illegible]blic health career were briefly touched on [illegible]his review culminating in Dr. Williams' Directorship of the New York Academy [illegible].

duced in quantity or entirely stopped when diarrhea appears or any other disturbance is manifested.

Colchicum exercises its pharmacologic effect on the capillaries and periarticular tissues, being capable in high dosage of causing arthritic attacks. This is of significance and is in harmony with the viewpoint that the gouty attack is an allergic reaction involving veins, capillaries and joints.

Nothing can be more unwise for the patient, than immediately after a cure of gout by this means to revert to the usual course of life. In the period after and between attacks the regulation of the mode of life is of prime importance. During this time, I believe, it is useful to put the patient on lemons and administer ½ to 1 teaspoonful of washed sulphur in water at night.

Sydenham concludes his famous dissertation on gout as follows: "As for a radical cure, this lies like Truth, at the bottom of a well; and so deep is it in the innermost recess of Nature that I know not when or by whom it will be brought forward into the light of day." These words still ring true today.

LIBRARY HOURS DURING THE SUMMER

As usual, the Library will be closed daily at 5 P. M. instead of 10:30 P. M., Wednesdays excepted, from June 15th to September 15th, inclusive. It will be open only on Wednesday evenings until 10:30 P. M.

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To the concluding words of Dr. Hartwell, in which there was an exhortation and a pledge: "Let us dedicate ourselves to the task of realizing his ideals and let us keep the name of Linsly Rudd Williams as a symbol of doing for others and making life a sweeter, better and happier experience," the audience gave full hearted assent by standing for a minute in silent tribute.

The Linsly R. Williams Memorial Meeting was arranged by a special subcommittee, who are also charged with the publication of the Linsly R. Williams Memorial Volume, in which will appear the addresses delivered at the memorial meeting, as well as other pertinent material bearing on the life of Dr. Williams.

PROCEEDINGS OF ACADEMY MEETINGS MARCH and APRIL

STATED MEETINGS

March 1

I. Executive Session—a. Reading of the Minutes; b. Election of Benefactor; c. Election of Officers; d. Election of Fellows and Members; e. Vote on Constitution and By-Laws.

II. Papers of the Evening—symposium: the problem of cavitation in pulmonary tuberculosis—a. From the medical standpoint, Edgar Mayer; b. From the surgical standpoint, Edward S. Welles, Saranac Lake; c. The roentgenological differential diagnosis of the tuberculous cavity, Ross Golden; d. Discussion, J. Burns Amberson, Jr.

THE HARVEY SOCIETY (in affiliation with the new york academy of medicine)

March 15

The Sixth Harvey Lecture, "The Significance of Morbid Process in the Fetus," George L. Streeter, Director, Department of Embryology, Carnegie Institute of Washington, Baltimore.

SECTION MEETINGS

section of surgery—March 2

I. Presentation of Cases—a. 1. Obstructive jaundice, Choledochoduodenostomy; 2. Acute osteomyelitis of the tibia; 3. Osteochrondroma of the femur, Gaston A. Carlucci; b. 1. Recurrent fibroma—five-year result, Paul C. Morton; c. Two cases illustrating paper, Charles W. Lester; d. One case illustrating paper, James R. Lincoln.

II. Papers of the Evening—a. Fractures of the odontoid process of the second cervical vertebra, James R. Lincoln; b. Chronic appendicitis and the right lower quadrant syndrome, Charles W. Lester.

III. General Discussion—Clay Ray Murray, Byron Stookey, Frederic W. Bancroft, Wm. Crawford White.

IV. Executive Session—Appointment of Nominating Committee.

SECTION OF DERMATOLOGY AND SYPHILOLOGY—March 6

I. PRESENTATION OF CASES FROM CITY HOSPITAL.

II. PRESENTATION OF MISCELLANEOUS CASES.

III. DISCUSSION OF SELECTED CASES.

IV. EXECUTIVE SESSION—Appointment of Nominating Committee.

JOINT MEETING—SECTION OF NEUROLOGY AND PSYCHIATRY and

THE NEW YORK NEUROLOGICAL SOCIETY—March 6

I. READING OF THE MINUTES.

II. PRESENTATION OF NEUROLOGICAL CASES OF UNUSUAL INTEREST.

III. GENERAL DISCUSSION.

IV. EXECUTIVE SESSION OF THE SECTION—Appointment of Nominating Committee.

JOINT MEETING UNDER THE AUSPICES OF THE NEW YORK ACADEMY OF MEDICINE, NEW YORK OBSTETRICAL SOCIETY and THE MEDICAL SOCIETY OF THE COUNTY OF NEW YORK

March 7

at The New York Academy of Medicine, 2 East 103rd Street

CONSTRUCTIVE ASPECTS OF THE ACADEMY OF MEDICINE REPORT ON MATERNAL MORTALITY—1. Resume of the Report, Harry Aranow; 2. Conclusions and Recommendations of the Report, George L. Brodhead; 3. Significance of the Report and the Measures Suggested for Carrying Out its Recommendations, George W. Kosmak. DISCUSSION—A. W. Bingham, East Orange, New Jersey; Clifford B. Lull, Philadelphia; Edward C. Podvin, New York City; S. S. Goldwater, Commissioner of Hospitals; John L. Rice, Commissioner of Health, and Thomas L. Parran, State Commissioner of Health.

COMBINED MEETING OF THE SECTION OF PEDIATRICS and the SECTION OF OBSTETRICS

AND GYNECOLOGY—March 8

I. EXECUTIVE SESSION—Appointment of Nominating Committee.

II. PAPERS OF THE EVENING—a. Morphinism in the new-born—A case report, R. Gordon Douglas (by invitation); b. Gas therapy in obstetrics and pediatrics, Paluel J. Flagg (by invitation). Discussed by Richard N. Pierson. c. Natimortality, Hugo Ehrenfest, St. Louis (by invitation). Discussed by William E. Studdiford.

III. GENERAL DISCUSSION.

SECTION OF HISTORICAL AND CULTURAL MEDICINE—March 14

I. READING OF THE MINUTES.

II. PAPERS OF THE EVENING—a. How the President, Thomas Jefferson, and Dr. Benjamin Waterhouse established vaccination as a public health procedure (with exhibit), Robert H. Halsey; b. Medicine among the American Indians (with lantern slides), Eric Stone, Providence, R. I. (by invitation).

III. GENERAL DISCUSSION.

IV. EXECUTIVE SESSION—Report of Nominating Committee.

SECTION OF ORTHOPEDIC SURGERY—March 16

I. Reading of the Minutes.

II. Presentation of Cases—a. Cineplastic amputation—case reports, Henry K. Kessler (by invitation); b. Sacroiliac strain secondary to lumbo-sacral fusion, Lewis C. Wagner; c. Living suture repair of fractures about the patella, Charles M. Gratz (by invitation).

III. Papers of the Evening—a. Vital capacity in spinal deformities, Kristian G. Hansson (by invitation); b. End results in the treatment of slipping of the upper femoral epiphysis, Maurice M. Pomeranz, Marian Frauenthal Sloane (by invitation).

IV. Discussion—Samuel Kleinberg, Armitage Whitman, Harry Finkelstein, Leo Mayer.

V. Executive Session—Appointment of Nominating Committee.

SECTION OF OPHTHALMOLOGY—March 19

I. Instruction Hour—7 to 8 o'clock—Ophthalmoscopy—lantern slides, Arthur J. Bedell.

II. Demonstration Hour—7:30 to 8:30 o'clock—a. Cases with divergence muscle anomalies; b. Ophthalmotrope, Wendell L. Hughes; c. Instruments used for testing muscle anomalies.

III. Section Meeting—8:30 to 10:30 o'clock—a. Executive Session; 1 Reading of minutes; 2. Appointment of Nominating Committee; b. Scientific Paper; 1. Divergence excess, Arthur Bielschowsky (by invitation). Discussers: 1. Herbert W. Wootton; 2. P. Chalmers Jameson (by invitation); 3. James W. White; 4. John H. Dunnington; 5. Le Grand H. Hardy.

SECTION OF MEDICINE—March 20

I. Reading of the Minutes.

II. Papers of the Evening—a. Further studies of the effect of tobacco on the peripheral vascular system, Irving Sherwood Wright, Dean Moffatt (by invitation); b. Insufficiently appreciated conceptions in the relation of the thyroid gland to Graves' disease, Henry B. Richardson; c. Clinical considerations concerning the detoxifying function of the liver, Armand J. Quick (by invitation); d. A case of diabetes of unusual type of insulin resistance, Bertram J. Sanger (by invitation) Henry E. Marks (by invitation); e. An epidemic (21 autopsies) of aestivoautumnal malaria in drug addicts transmitted by hypodermic syringe, Milton Helpern (by invitation).

III. General Discussion.

IV. Executive Session—Appointment of Nominating Committee.

SECTION OF GENITO-URINARY SURGERY—March 21

I. Reading of the Minutes.

II. Presentation of Instrument—A new female urethroscope, Paul M. Butterfield.

III. Papers of the Evening—a. Calculous anuria, George F. Cahill; b. Some ureteral problems, John R. Caulk, St. Louis (by invitation). Discussion: Edwin Beer, Harold H. Gile (by invitation), Edward L. Keyes, Nathaniel P. Rathbun.

IV. General Discussion.

V. Executive Session—Appointment of Nominating Committee.

SECTION OF OTOLARYNGOLOGY—March 21

I. Reading of the Minutes.

II. Appointment of Nominating Committee.

III. Case Presentations—a. Prickle cell epithelioma of the ear with involvement of the facial nerve, Ward C. Denison. Discussion: T. J. Harris. b. Otitic hydrocephalus, Clarence H. Smith. Discussion: S. P. Goodhart.

IV. Papers of the Evening—a. The window operation for hematoma auris and perichrondritis with effusion, Robert C. Howard. Discussion: Ralph Almour, J. Coleman Seal. b. Avulsion of the vocal cord, John M. Loré. Discussion: David H. Jones, Charles J. Imperatori, M. C. Myerson, L. Glushak, E. Josephson. c. A simple surgical method of dealing with calculi in the submaxillary salivary duct, August L. Beck. Discussion: Lee M. Hurd, Theodor Blum.

V. General Discussion.

AFFILIATED SOCIETIES

NEW YORK ROENTGEN SOCIETY IN AFFILIATION WITH THE NEW YORK ACADEMY OF MEDICINE
March 19

I. 8:00 to 8:30 p.m.—Demonstration and discussion of interesting cases.

II. 8:30 p.m.—Bone changes in cases of disturbance in lipoid metabolism, Leopold Jaches.

NEW YORK MEETING OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE UNDER THE AUSPICES OF THE NEW YORK ACADEMY OF MEDICINE—March 21

I. *In vivo* and *in vitro* cultivation of the virus of rift valley fever, R. S. Saddington (Read by T. M. Rivers).

II. Distribution of virus of louping-ill in blood and brain of intranasally infected mice, G. L. Fite, L. T. Webster.

III. Ultra-filtration experiments with the encephalitis virus from the St. Louis epidemic, J. H. Bauer, G. L. Fite, L. T. Webster.

IV. Formation of agglutinins with lymph nodes, P. D. McMaster, S. S. Hudack.

V. Reaction of the rabbit to vaccine virus, L. Pearce, P. D. Rosahn, C. K. Hu.

VI. Differential ovarian responses after injections of follicle-stimulating and pregnancy urine in young female rats, P. E. Smith, E. T. Engle, H. H. Tyndale.

VII. Gametokinetic action of extracts of follicle-stimulating urine, P. E. Smith, E. T. Engle, H. H. Tyndale.

VIII. Action of pregnancy urine extract (Follutein) on external genitalia of female guinea pigs, G. N. Papanicolaou, E. A. Falk.

IX. Inversion of the P wave in the third lead of electrocardiograms with a large Q-3 wave, C. Shookhoff, A. H. Douglas (Introduced by H. Gold).

NEW YORK PATHOLOGICAL SOCIETY IN AFFILIATION WITH THE NEW YORK ACADEMY OF MEDICINE—March 22

I. Presentation of Cases.

II. Papers of the Evening—a. Dilatation of the pulmonary artery; 1. Idiopathic; 2. Associated with cardiac anomalies, B. S. Oppenheimer; b. Pathology of measles with special reference to pneumonia, L. W. Smith; c. A review of recent studies of yellow fever, W. A. Sawyer (by invitation).

STATED MEETINGS

Program arranged in cooperation with the New York Pathological Society.
April 5

I. Executive Session—a. Reading of the Minutes; b. Election of Fellows and Members.

II. Papers of the Evening—symposium: recent progress in leukemia research; a. Experimental aspects, Maurice N. Richter (20 min.), Jacob Furth (20 min.); b. Pathology, Richard H. Jaffe, Chicago (30 min.); c. Clinical and therapeutic aspects, Lloyd F. Craver (20 min.); d. Discussion, Francis C. Wood, Nathan Rosenthal.

THE HARVEY SOCIETY (in affiliation with the new york academy of medicine)
April 19

The Seventh Harvey Lecture, "Filtrable Viruses with Particular Reference to Psittacosis," Thomas M. Rivers, Member of the Rockefeller Institute.

SECTION MEETINGS

section of dermatology and syphilology—April 3

I. Presentation of Cases from—Beth-Israel Hospital, Seaview Hospital.

II. Presentation of Miscellaneous Cases.

III. Discussion of Selected Cases.

IV. Executive Session.

V. Nomination of Section Officers and One Member of Advisory Committee.

joint meeting section of neurology and psychiatry and the section of dermatology and syphilology—April 10

I. Reading of the Minutes.

II. Papers of the Evening—a. Psychogenic aspects of skin diseases, Joseph Klauder; b. Remarks on the psycho-physiology of the skin, Paul Schilder.

III. Discussion—Charles M. Williams, Abraham Walzer, Smith Ely Jelliffe, J. Ramsay Hunt.

IV. Executive Session of the Section of Neurology and Psychiatry—Nomination of officers and two members of the Advisory Committee.

combined meeting of the section of pediatrics and the section of surgery—April 12

I. Executive Session—Nomination of Section Officers and One Member of Advisory Committee.

II. Papers of the Evening—a. Two cases of pneumococcus peritonitis, John V. Bohrer; b. One case of pneumococcus peritonitis, Philip D. Allen; c. Pneumococcus peritonitis from the pediatric viewpoint, Murray H. Bass; d. Pneumococcus peritonitis from the surgical viewpoint, Edward Donovan; e. Pneumococcus peritonitis in nephrosis, John D. Lyttle. Discussion: Harold Neuhof, Bernard Denzer, William Heeks (by invitation).

section of ophthalmology—*Monday* Afternoon and Evening, April 16

I. Demonstration of the mechanism and use of the ophthalmo-Eikonometer, an *instrument* for determining Aniseikonia (i. e., differences in the size and shape of ocular images), 3 to 5 o'clock.

II. Instruction Hour, 7 to 8 o'clock—A new method of microanatomy of the eye; 1. Comparative anatomy of the angle of the anterior chamber in living and dead eyes, Manuel Uribe Troncoso (by invitation), Ramon Castroviejo (by invitation).

III. Demonstration of patients corrected for aniseikonic defects, 7:30 to 8:15 o'clock—Slit Lamp Studies, Milton L. Berliner, Isadore Goldstein, Wendell L. Hughes, Girolamo Bonaccolto (by invitation).

IV. Papers of the Evening, 8:15 to 10 o'clock—a. The nature of fixation and its effect on the physiology of visual acuity, Francis H. Adler (by invitation); b. Aniseikonia —Differences in size and shape of ocular images, Mr. Julius Neumueller, B.S., O.D. (by invitation); c. Examination and treatment of aniseikonia, Mr. Leo F. Madigan (by invitation). Discussion: Elmer H. Carleton (by invitation), Wendell L. Hughes, Mr. Adelbert Ames, Jr. (by invitation).

V. Executive Session—Reading of the Minutes; Nomination of Section Officers and one member of Advisory Committee.

COMBINED MEETING OF THE SECTION OF GENITO-URINARY SURGERY and the SECTION OF MEDICINE—April 18

I. Reading of the Minutes.

II. Papers of the Evening—perinephritis and perinephritic abscess; 1. From the Medical standpoint, Henry B. Richardson; 2. From the urologic standpoint, Henry G. Bugbee. Discussion to be opened by Nathaniel P. Rathbun.

III. General Discussion.

IV. Executive Session—Section of Medicine, Nomination of Section officers and one member of the Advisory Committee; Section of Genito-Urinary Surgery, Nomination and election of Section officers and one member of the Advisory Committee; *No May Meeting of this Section will be held.*

SECTION OF OTOLARYNGOLOGY—April 18

I. Reading of the Minutes.

II. Executive Session—Nomination of Section officers and one member of Advisory Committee.

III. Case Presentations—a. Presentation of patients with laryngeal carcinoma treated by roentgen rays, I. Seth Hirsch. Discussion: Ira I. Kaplan, Maurice Lenz. b. A case of myoblastoma of the larynx, Louis Kleinfeld. Discussion: Paul Klemperer.

IV. Papers of the Evening—a. Roentgenologic interpretation of cysts and tumors of the upper jaw, S. Fineman. Discussion: P. Klemperer. b. Cancer of the larynx; some conclusions derived from personal experience, Joseph C. Beck (by invitation), M. Reese Guttman, Chicago (by invitation). Discussion opened by: Caesar Hirsch, formerly medical director, nose and throat service, Marien Hospital, Stuttgart, Germany (by invitation). Discussion continued by: Charles J. Imperatori, Duncan Macpherson, Robert E. Buckley.

SECTION OF ORTHOPEDIC SURGERY—April 20

I. Reading of the Minutes.

II. Presentation of Cases—a. Some new apparatus in the treatment of fractures, George W. Hawley, Bridgeport (by invitation); b. A simple method for reduction of fracture dislocations of the vertebrae, especially those associated with spinal cord injuries, Byron Stookey; c. Cases demonstrating a new method of internal fixation in fractures of the neck of the femur using Kirschner wires, David Telson (by invitation).

III. Paper of the Evening—An analysis of end results in the treatment of central fractures of the neck of the femur and of the trochanteric region, J. S. Speed, Memphis (by invitation).

IV. General Discussion.

V. Executive Session—Nomination of Section officers and one member of Advisory Committee.

SECTION OF OBSTETRICS AND GYNECOLOGY—April 27

Program Arranged by the Obstetrical Staff of The Nursery and Child's Hospital.

(Meeting Postponed from April 24)

I. Reading of the Minutes.

II. Presentation of Cases—Rupture of a chocolate cyst with acute symptoms, Ogden F. Conkey (by invitation). Discussion: Howard C. Taylor, Jr.

III. Papers of the Evening—a. Placenta praevia—analysis of 146 cases, James P. Marr (by invitation). Discussion: Albert H. Aldridge. b. Pentobarbital analgesia—report of 200 cases, James P. Boylan (by invitation). Discussion: C. F. Jellinghaus, V. G. Damon (by invitation). c. Latzko-extra-peritoneal caesarean section—study of 79 cases, Henry T. Burns (by invitation). Discussion: Samuel J. Scadron.

IV. General Discussion.

V. Executive Session—Nomination of Section officers and one member of Advisory Committee.

AFFILIATED SOCIETIES

NEW YORK ROENTGEN SOCIETY IN AFFILIATION WITH THE NEW YORK ACADEMY OF MEDICINE

Monday Evening, April 16, at 8:00 o'clock

I. 8:00 to 8:30 p.m.—Demonstration and discussion of interesting cases.

II. 8:30 p.m.—Certain aspects of roentgenology of the spine from the orthopedic viewpoint, R. W. Lewis.

III. General Discussion—To be opened by Armitage Whitman (by invitation).

IV. Executive Session.

NEW YORK MEETING OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE UNDER THE AUSPICES OF THE NEW YORK ACADEMY OF MEDICINE—April 18

I. Studies of incurable rickets. Respective role of the local factor and Vitamin D in healing, A. E. Sobel, A. Goldfarb, B. Kramer.

II. Experiments on Vitamin G concentration and possible supplementary relationships with Vitamin G deficient diet, J. W. Page, Jr. (Introduced by H. C. Sherman.)

III. Protection afforded by certain vegetable oils against nutritional encephalomalacia of chicks, A. M. Pappenheimer, M. Goettsch.

IV. Measurement of circulation time from antecubital veins to pulmonary capillaries, W. M. Hitzig. (Introduced by B. S. Oppenheimer.)

V. Pacinian corpuscles in the mesentery and their relation to the vascular system, G. D. Gammon, D. W. Bronk.

VI. Tuberculosis induced in the tadpole by feeding, J. F. Nonidez, M. C. Kahn.

VII. Globulin extract of immune adult serum in prophylaxis of measles, S. Karelitz. (Introduced by B. Schick.)

VIII. Prophylactic vaccination against intracranial complications following pneumococcus type III mastoiditis, G. Schwartzman, J. L. Goldman, C. Herschberger.

IX. New serum therapy for non-specific ulcerative colitis, G. Schwartzman, A. Winkelstein.

This was the annual meeting of the Society. Reports of tellers, secretary and treasurer were read.

RECENT ACCESSIONS TO THE LIBRARY

Abraham, J. J. Lettsom, his life, times, friends and descendants.
London, Heinemann, 1933, 498 p.
Association for research in nervous and mental disease. Localization of function in the cerebral cortex.
Balt., Williams, 1934, 667 p.
Atkinson, D. T. External diseases of the eye.
Phil., Lea, 1934, 704 p.
Beaumont, G. E. & Dodds, E. C. Recent advances in medicine. 7. ed.
London, Churchill, 1934, 485 p.
Best, H. Blindness and the blind in the United States.
N. Y., Macmillan, 1934, 714 p.
Brocq-Rousseu, D. & Roussel, G. Le sérum normal.
Paris, Masson, 1934, 363 p.
Byrne, J. G. Clinical studies on the physiology of the eye.
London, Lewis, 1934, 144 p.
Calmette, A.; Boquet, A. & Nègre, C. L. A. Manuel technique de microbiologie et sérologie. 3. éd.
Paris, Masson, 1933, 759 p.
Codman, E. A. The shoulder; rupture of the supraspinatus tendon and other lesions in or about the subacromial bursa.
Boston, [The Author?], 1934, 513 p.
Devine, H. Recent advances in psychiatry. 2. ed.
Phil., Blakiston, 1933, 364 p.
Dioscorides Anazarbeus, P. The Greek herbal of Dioscorides.
Oxford, Johnson, 1934, 701 p.
Feinberg, S. M. Allergy in general practice.
Phil., Lea, 1934, 339 p.
Fischer, G. Local anesthesia in dentistry. 4. ed.
London, Kimpton, 1934, 222 p.
Franklin, K. J. A short history of physiology.
London, Bale, 1933, 122 p.
Gadow, H. F. The evolution of the vertebral column.
Cambridge [Eng.], University Press, 1933, 355 p.
Gardner, A. D. Bacteriology, for medical students and practitioners.
London, Milford, 1933, 276 p.
Gask, G. E. & Ross, J. P. The surgery of the sympathetic nervous system.
Balt., Wood, 1934, 163 p.
Gastinel, P. & Pulvenis, R. La syphilis expérimentale.
Paris, Masson, 1934, 243 p.
Goodall, E. W. A short history of the epidemic infectious diseases.
London, Bale, 1934, 113 p.
Gutierrez, R. The clinical management of horseshoe kidney.
N. Y., Hoeber, 1934, 143 p.
Hanke, M. T. Diet and dental health.
Chic., Univ. of Chic. Press, [1933], 235 p.

Henning, N. Die Entzündung des Magens.
Leipzig, Barth, 1934, 235 p.
Howard, R. & Perry, A. C. The practice of surgery. 4. ed.
Balt., Wood, 1933, 1338 p.
Huddleson, I. F. Brucella infections in animals and man.
N. Y., Commonwealth Fund, 1934, 108 p.
Huxley, J. S. & De Beer, G. R. The elements of experimental embryology.
Cambridge [Eng.], University Press, 1934, 514 p.
Jungmichel, G. Alkoholbestimmung im Blut.
Berlin, Heymann, 1933, 124 p.
Key, J. A. & Conwell, H. E. The management of fractures, dislocations, and sprains.
St. Louis, Mosby, 1934, 1164 p.
Kovacs, R. Nature, M.D.
N. Y., Appleton-Century, 1934, 181 p.
Landsteiner, K. Die Spezifizität der serologischen Reaktionen.
Berlin, Springer, 1933, 123 p.
Leriche, R. & Stricker, P. L'artériectomie dans les artérites oblitérantes.
Paris, Masson, 1933, 194 p.
Lovejoy, E. P. Certain Samaritans. New ed.
N. Y., Macmillan, 1933, 344 p.
Mitchell, A. C. G. & Zemansky, M. W. Resonance radiation and excited atoms.
Cambridge [Eng.], University Press, 1934, 338 p.
Morse, W. R. Chinese medicine.
N. Y., Hoeber, 1934, 185 p.
Muir, R. Text-book of pathology. 3. ed.
Balt., Wood, 1933, 957 p.
National organization for public health nursing. Committee on field studies and administrative practice. Survey of public health nursing; administration and practice.
N. Y., Commonwealth Fund, 1934, 262 p.
Newsholme, (Sir) A. & Kingsbury, J. A. Red medicine; socialized health in Soviet Russia.
Garden City, Doubleday, 1933, 324 p.
Nicolaysen, J. Kirurgien i Norge i det 19de århundre.
Oslo, Centraltrykkeriet, 1933, 127 p.
Nissen, N. I. Studies on alimentary lipaemia in man.
Copenhagen, Levin, 1933, 176 p.
Obermeyer, H. Stop that smoke.
N. Y., Harper, 1933, 289 p.
Oldham, F. Thomas Young, F.R.S., philosopher and physician.
London, Arnold, 1933, 159 p.
Pachon, V. & Fabre, R. Clinical investigation of cardiovascular function.
London, Paul, 1934, 252 p.
Pal, J. Die Tonuskrankheiten des Herzens und der Gefässe.
Wien, Springer, 1934, 228 p.

Park, W. H. & Williams, A. W. Pathogenic microörganisms. 10. ed.
Phil., Lea, [1933], 867 p.
Pattee, A. F. Practical dietetics. 19. ed.
Mt. Vernon, Pattee, 1933, 881 p.
Payr, E. Gelenksteifen und Gelenkplastik.
Berlin, Springer, 1934, pt. 1.
Pearl, R. Constitution and health.
London, Paul, 1933, 97 p.
Philips' (N. V.) gloeilampenfabrieken, Eindhoven. X-ray research and development. A selection of publications of the Philips x-ray research laboratory.
London, Hanbury, [1934?], 204 p.
Renshaw, S.; Miller, V. L. & Marquis, (Mrs.) D. (Postle). Children's sleep.
N. Y., Macmillan, 1933, 242 p.
Seaver, G. Edward Wilson of the Antarctic.
London, Murray, [1934], 301 p.
Seldin, H. M. Practical anesthesia for dental and oral surgery.
Phil., Lea, 1934, 525 p.
Stinchfield, S. M. Speech disorders.
London, Paul, 1933, 341 p.
Textbook (A) of the practice of medicine. Edited by F. W. Price. 4. ed.
London, Milford, 1933, 1995 p.
Thomson, J. The clinical study and treatment of sick children. 5. ed.
Edinburgh, Oliver, 1933, 1075 p.
Traité élémentaire d'exploration clinique médicale (technique et séméiologie). Publié sous la direction de E. Sergent.
Paris, Masson, 1934, 1176 p.
de Vries, W. M. Atlas of selected cases of pathological anatomy.
Amsterdam, de Bussy, 1933, 73 p.
Wakeley, C. P. G. & Hunter, J. B. Rose and Carless' manual of surgery. American (14.) ed.
Balt., Wood, 1933, 1408 p.
Walker, K. M. The enlarged prostate and prostatic obstruction. 2. ed.
London, Milford, 1933, 223 p.
Watson, F. The life of Sir Robert Jones.
London, Hodder, 1934, 327 p.
Wollaston, A. F. R. Letters and diaries.
Cambridge [Eng.], University Press, 1933, 261 p.

AMENDMENT TO BY-LAWS PASSED AT A STATED MEETING OF THE ACADEMY HELD MARCH 1, 1934

ARTICLE X, SECTION 7

as prepared by the counsel of the Academy
and presented by the Trustees.

SECTION 7. *Executive Committee.* The Board of Trustees by resolution passed by a majority of the whole Board, may designate two or more of their number to constitute an Executive Committee to serve during the pleasure of the Board. During the interval between the meetings of the Board of Trustees the Executive Committee shall possess and may exercise all of the powers of the Board of Trustees conferred by these by-laws or otherwise, except as limited from time to time by resolution of the Board of Trustees, including power to authorize the seal of the Corporation to be affixed to all papers which may require it. The Committee shall adopt its own rules of procedure, and shall meet when and where and according to the notice provided by such rules. It shall keep a record of all its proceedings and report the same to the Board of Trustees.

Vacancies in the Executive Committee shall be filled by the Board of Trustees, but during the temporary absence or inability to act of a member of the Executive Committee, the remaining members may appoint a member of the Board of Trustees to act in his place. The members of the Committee shall elect one of their number as Chairman, and may elect another member as Vice-Chairman. The Secretary or any other official of the Corporation shall perform the duties of Secretary to the Committee at its request. A majority of the Committee shall constitute a quorum.

FELLOW AND MEMBERS AND ASSOCIATE ELECTED MARCH 1, 1934

Fellow:

Birt Lee Browning........................Grand Ave., Balaville, N. Y.

Members:

Ruth Morris Bakwin................................132 East 71 Street
Sandor Lorand................................115 East 86 Street
Frances Emily Shields................................5 East 57 Street
Russell C. Kimball............................52 Remsen St., Brooklyn
Willis Sackett Knighton............................40 East 61 Street
George Eaton Daniels ....454 Riverside Drive
Lester Reginald Tuchman............................101 West 58 Street
Bertram David Lewin................................25 Fifth Avenue

Associate:

Robert Keith Cannan, M.Sc............................477 First Avenue

FELLOWS AND MEMBERS ELECTED

APRIL 5, 1934

Fellows:

Jacob E. Holzman..1075 Park Avenue
Otho C. Hudson..Hempstead, L. I.

Members:

John L. Rice..Department of Health
Louis Wender..Hastings-on-Hudson, N. Y.
Olin Everett Farley..140 East 54 Street
Phil Hawkins Neal..136 East 65 Street
Joseph Benjamin Stenbuck..1165 Park Avenue
Seymour H. Silvers..2 East 54 Street
Peter G. Denker..139 East 66 Street
Virgil G. Damon..1088 Park Avenue
Tibor de Cholnoky..85 East 84 Street
John Corran McCauley, Jr..116 East 63 Street
Gustave Aufricht..103 East 86 Street

DEATHS OF FELLOWS OF THE ACADEMY

Cleveland, Clement, M.D., 11 West 11 Street, New York City; graduated in arts from Harvard University in 1867 and in medicine from the College of Physicians and Surgeons, New York City, in 1871; elected a Fellow of the Academy May 1, 1879; died, April 16, 1934. At the time of his death he was the oldest living Fellow of the Academy. He was a Trustee of the Academy from 1897 to 1900. Dr. Cleveland was a Fellow of the American College of Surgeons. He was formerly President of the American Gynecological Society and of the New York Obstetrical Society. At various times he was connected with Woman's Hospital and Memorial Hospital and from 1882 to 1915 he was Attending Surgeon and Surgical Director of City Hospital.

Ely, Albert Heman, M.D., Cold Spring Harbor, Long Island, New York; graduated in medicine from the College of Physicians and Surgeons in 1888; elected a Fellow of the Academy March 1, 1894; died April 26, 1934. Dr. Ely was a Fellow of the American Medical Association and a member of the County and State Medical Societies, the New York Obstetrical Society and the Alumni Association of St. Luke's Hospital. He was at one time associated with Roosevelt and City hospitals. He was one of the founders of Southampton Hospital where he was consulting surgeon at the time of his death.

PACKARD, MAURICE, Ph.B., M.D., 17 West 70 Street, New York City; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1900; elected a Fellow of the Academy February 4, 1909; died, March 14, 1934. Dr. Packard was a Fellow of the American Medical Association, a member of the County and State Medical Societies, the New York Pathological Society and the Brooklyn Hospital Alumni Association. He was Consulting Physician to Joint Diseases, Broad Street and Jewish Maternity hospitals and Physician to Gouverneur Hospital.

PILGRIM, CHARLES WINFIELD, M.D., Central Valley, New York; graduated in medicine from Bellevue Hospital Medical College in 1881; elected a Fellow of the Academy October 6, 1898; died May 3, 1934. Dr. Pilgrim was a member of the County and State Medical Societies, the American Psychiatric Association and the Psychiatric Society of New York. Dr. Pilgrim was a pioneer in the development of the out-patient department in connection with the State hospitals and was one of he earliest advocates of mental clinics and social service work among the insane. He also urged extension of the parole system among the insane. In recognition of the outstanding service performed by Dr. Pilgrim in the State hospitals and among the insane of New York State, the New York State Legislature in 1929 authorized construction of the Charles W. Pilgrim State Hospital at Brentwood, New York, which will be the largest asylum in the world when it is completed.

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October 23 to November 3, 1933

*Round Table Conference on Diabetes Mellitus**

DIETARY TRENDS

ROLLIN T. WOODYATT
Chicago

The history of diabetes is marked by the recurrence of certain ideas which rise, decline and disappear, only to make a new appearance and go through a similar cycle again in an altered form, and a new generation. This is notably true of trends in diet. Certain conceptions recur more often and tend to stay with us longer and longer until we come to regard them as permanent.

Caloric Magnitude of the Diet. The conception that overnutrition is detrimental to health in the presence or absence of diabetes, and in its presence, specifically so, appears to be true. An extension of this idea is to the effect that in diabetes some degree of undernutrition favors the preservation of natural carbohydrate tolerance or of its partial rebuilding or restoration in cases in which restoration is possible. When tolerance has sunk to the vanishing point and remained there in spite of all efforts to build it up, for a long enough time, then, until future discoveries change the picture, we must consider the natural tolerance dead, burnt out or beyond recall. When this stage is reached, there is no longer hope

*Delivered October 30, 1933 before the joint meeting of The New York Academy of Medicine and the Medical Society of the County of New York.

of preserving or rebuilding natural tolerance by any present day method. However, even in this situation it is held that undernutrition may increase the effectiveness of the unit of insulin, permit one to use a smaller dose, and make the management generally smoother and safer. Joslin recommends as a general rule that, in the case of a diabetic patient of a given age, height and sex, the diet should be restricted enough to keep the body weight 10 per cent below the average for normal subjects of the same age, height and sex, as shown on standard statistical tables. Probably if this rule were followed in every case the advantages gained would outweigh occasional disadvantages. There are exceptions to every rule. Still, all things considered, most writers agree that overnutrition is undesirable and that it is better to keep a patient spare and under—rather than overnourished. Accordingly, the calorie magnitude of the diet should be adjusted to keep the body weight at the level desired.

Protein Limitation. Another conception that has returned persistently through the years and has come to be looked on as fairly established, is that an excess of protein is undesirable. Here again opinions will vary for some time to come as to the desirable limits of protein restriction. For adults, an allowance of somewhere between 0.75 and 1.25 gm. per kilo per day might meet the approval of most modern writers. For growing children a larger allowance is recommended by pediatricians, *i. e.*, 2.0 to 2.5 gm. per kilo.

Carbohydrate and Fat. Having fixed the number of total calories and the quantity of protein (which determines the number of protein calories) there will be a calorie remainder to be supplied by carbohydrate and fat, and whatever quantity we use of one will determine the quantity of the other, for if the total non-protein calories were 1500 and if we used 150 gm. of carbohydrate, producing 600 calories, we would have to use 100 gm. of fat to make up the 900 calorie balance. The question then arises as to how much of each may best be employed—or stating it more simply, how much of either.

In some of the older rigid diets or diets of the types associated with the names of Newburgh and Marsh or Petrén of Sweden, the carbohydrate has been reduced to a minimum. In some of the diets of Newburgh and Marsh it has represented but 5 to 10 per cent of the non-protein calories, the remainder being supplied by fat, and this implies that the fat outweighs the carbohydrate roughly 8 or 4 to 1. However, the total quantity of fat or carbohydrate depends not merely on the relative proportions but also on the total magnitude of the diet. With a diet containing 1700 non-protein calories the above ratios would indicate 20 to 40 gm. carbohydrate and 170 to 180 gm. fat, whereas, with only 1000 non-protein calories, they would indicate not over 105 gm. fat. All such diets are sometimes referred to as "high fat" diets without regard for magnitudes but only the larger ones are absolutely high in fat. The smaller are actually low in fat. But they all have in common *low carbohydrate.*

In contrast with the above are diets containing larger quantities of carbohydrate, and all other factors remaining the same, correspondingly smaller amounts of fat. They are referred to by some as "high carbohydrate" diets or by others as "low fat" diets—depending on the author's idea as to whether elevation of the carbohydrate or depression of the fat is the more important consideration. The employment of diets of this description is by no means a recent innovation. Allen states that according to Stokvis milk was recommended for diabetes by almost all writers in the 18th century, and that Richardson credits a "Dr. Smart of Edinburgh" with priority in the use of a formal "milk cure." In any event, in 1874 Donkin published a paper on diabetes mellitus successfully treated with skimmed milk, which became widely known and started the movement. He gave diets of low calorie value consisting almost entirely of skimmed milk. One hundred grams of skimmed milk may contain 5 gm. carbohydrate, 3 gm. protein, 0.3 gm. fat, and about 35 calories. To provide, let us say 1750 calories, the quantity of skimmed milk required would be 5 liters. This would contain 250 gm. carbohy-

drate, 150 gm. protein and 15 gm. fat (C:F ratio 17:1). A whole milk diet of the same calorie value would contain approximately 125 gm. carbohydrate, 75 gm. protein and 100 gm. fat (C:F ratio 1.25:1). So milk diets may have compositions corresponding closely with those of modern "high carbohydrate" diets.

Following Donkin, many writers employed his methods with good results, and "milk cures" in one form and another remained in use for a long time. They have been recommended as useful in some situations by such noted authorities as Naunyn (1896), and von Noorden (1898 to 1910), and were reindorsed by Winternitz and Strasser (1899). Again, as late as 1915 their beneficial effects were pointed out by Williamson and by La Farge, the latter believing that the lactose in milk was particularly well tolerated, and that it increased the tolerance for other carbohydrates. But milk cures never enjoyed a vogue in the United States, although they were doubtless tried by individuals.

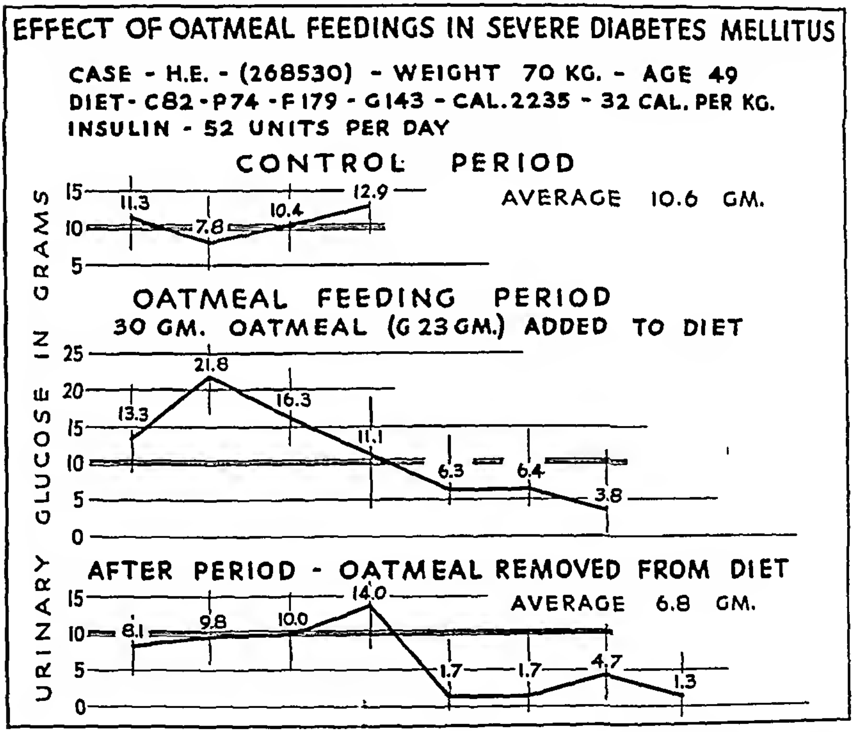
The von Düring vegetable cure first described in 1868, consisted in the administration of rice or other cereals, some bread, fruits, milk, wine and a rather liberal allowance of meat. The von Düring diets were low in calories, high in carbohydrate, moderate in protein and low in fat. Their composition can not be stated exactly. Beneficial results were often obtained by von Düring and others who followed his methods.

The Mossé "potato cure" so called, first described in 1898, involved the use of liberal or even enormous quantities of potato. This method enjoyed a vogue in France. The alleged benefits were attributed to specific properties of the potato. We may allow for gross exaggerations of the percentage of cases in which beneficial results were really obtained by the Mossé method, and still understand how a diet composed more or less exclusively of potatoes may be high in carbohydrate, low in protein, low in fat, and easily low in total calories. More than 2 kilos of boiled potatoes would be required to provide 1800 calories. In the light of present day knowledge there is little

doubt that the reputation of the Mossé potato cure rested on the occasional observation of the same type of results as those observed with the Donkin or Düring "cures."

The "oatmeal or oat cure" as described by von Noorden (Zuckerkrankheit, 5th ed., p. 312, 1910) consisted of 250 gm. oatmeal, 200 to 300 gm. butter, and 100 gm. of vegetable protein or 5 to 8 eggs. It might therefore, contain C.161, P.140, F.185 to 270 gm. and yield in round numbers 2900 to 3700 calories, depending on the quantity of butter employed. With the eggs in place of the plant albumin, the protein would be 30 to 50 gm. less, and the fat 30 to 50 gm. higher, so that the fat might rise to the high extreme of 320 gm. Such a ration would have to be described as a high calorie, high carbohydrate, high fat diet, with moderate protein (70 to 140 gm.). The fat exceeds the carbohydrate sometimes as much as 2 to 1. Concerning the "oat cure," von Noorden says, "It is of extraordinary practical significance; the theory of its action however, presents a most difficult problem. I discovered its significance quite accidentally. Some patients in my clinic were troubled with severe disorders of the stomach and bowel. I therefore gave them oatmeal gruel. Remarkably enough, the glycosuria did not increase, but became much less than it had been before on the most rigid diet. This became the starting point for further researches which were continued most carefully for two years before I ventured to publish the paradoxical facts." *Several days on a rigid diet and 1 or 2 days on a low vegetable diet usually preceded the oatmeal diet,* which was then given for 3 or 4 days and followed by 1 or 2 vegetable days. Continuing the quotation—"In suitable favorable cases it is observed that in the beginning of the oat cure the glycosuria frequently rises somewhat; but after several days it sinks decidedly, and with it or even to a relatively greater degree, the ketonuria sinks. Often even during the first oat period one obtains entirely sugar free urine; if this is not the case, one may still count on it with fair certainty during the following vegetable days." "Whoever considers the tables without prejudice must admit that results were

obtained with respect to glycosuria and ketonuria that one would not have thought were possible before. *Unfortunately, there are relatively few cases in which the results are so surprisingly favorable;* in other cases the results were entirely absent or only partial." In 1910 von Noorden believed that the favorable results obtained with other cures—Donkin's von Düring's, Mossé's, etc., were due to the use of simple rations containing but one kind of carbohydrate, and that the oat cure was similar in this respect, but that it was superior to others, and owed its superiority to specific properties of oats.



The oatmeal "cure" led to studies of various cereals and cereal diets by Falta, Porges, Salomon and others. Porges discarded von Noorden's belief in the specificity of oats, but held to the view that it was necessary to use but a single cereal or carbohydrate. However, Falta effectually dispelled this misconception by obtaining the same results with various cereals and cereal mixtures. He stress-

ed the importance of *protein restriction* in kind and quantity. In 1911 Klemperer appears to have shown that results quite analogous to those observed in the course of an oat cure could be produced by the use of glucose alone, and it is remarkable how many years had elapsed, and how much work had been done with complicated mixtures and intricate theories before pure sugars were experimentally tested. The literature on this subject continued up to the time of the war. It was almost entirely European.

The following years saw a rapid development of research in this country, especially in the field of metabolism and diabetes, but interest ran in other channels. There was an inclination toward skepticism concerning the phenomena said to occur in the course of "cures" and to think that there was nothing mysterious about them. I erred for one in averring at one time that their reputation rested on faulty measurements of the glucose supply, in a paragraph quoted by Graham Lusk. Allen said also in 1919—"The rationale of the carbohydrate 'cures' appeared mysterious when diabetes was regarded as a deficiency of carbohydrate assimilation, but becomes clear with the understanding of diabetes as a general disorder of the metabolism." He felt at that time that the preliminary undernutrition and limitation of fat and protein accounted for all the alleged results.

Before proceeding, let us look at a chart (see Figure) which shows the phenomenon under discussion. A male patient with severe diabetes who had been for nine years on insulin treatment and had served repeatedly in feeding experiments, was forty-nine years old, 5 ft. 9 in. tall, and weighed 154 lbs. or 70 kg. The patient was not confined to bed but did light and standardized physical work. The diet contained carbohydrate 82 gm., protein 74 gm., fat 179 gm., calories 2235 (32 cal. per kg.). The insulin was adjusted to allow the excretion of an easily measurable quantity of sugar. The dose of insulin was 52 units. He was kept on this diet and insulin dose until for 10 days the sugar excretion had varied not more than 3 gm. above or below a mean of 10. Then, as a simple superposition on his

regular diet, he was given 30 gm. oatmeal daily for 7 days, in which all other factors remained the same. This quantity of oatmeal contains 113 calories and 23 gm. of glucose equivalents. The oatmeal period was followed by an after period in which conditions were the same as before. It will be seen that the sugar excretion rose temporarily and then fell below the original level, as described by von Noorden during an oat cure. After withdrawal of the oatmeal the glycosuria returned to its former level for 3 days, then disappeared except for a trace.* It may be noted that the patient was of nearly average weight for his height and not undernourished during the experiment. The addition of the oatmeal increased the calories by 113. The diet was high in fat throughout and of a type that the patient had used for years. The effect would have to be ascribed simply to the *addition* of the cereal or, as it is possibly safe to say, the simple *addition of carbohydrate.*

At the end of the experiment the patient was apparently utilizing (burning, storing or both) 32 gm. more glucose than he had been before, although the insulin dosage remained the same. If, as Klemperer held, the same type of result may be obtained with feedings of glucose alone, the effect would seem to be that of the *carbohydrate.* But during the fore period there was at all times an excess of sugar in the body, and we might wonder why this was less available to the body than administered sugar. Although several hypotheses have been advanced to explain the phenomenon, it still presents an interesting problem for further investigation.

Now, resuming the narrative, after the war dietary trends in this country were generally toward low calorie, low protein diets in which the total quantity of fat was moderate, but usually higher than the carbohydrate. Meanwhile, Falta, Porges and others in Europe continued the use of cereal diets. With the advent of insulin in 1921,

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*By the Folin-Berglund method of sugar determination employed the fractions to the right of the decimal are within normal limits.

American writers still adhered to the types of diets that they had been using, although insulin now permitted them wider latitude. In 1926, Geyelin, working with diabetic children, had had certain cases in which it was difficult to control the glycosuria without inducing insulin reactions. In view of the emphasis that had been laid on the harmful effect of fat in this country, it was natural to consider the possibility that the fat in his diets might be to blame. He therefore reduced the amount of fat and supplied the necessary calories with carbohydrate, prepared to use larger insulin doses, but as he states, he was "surprised" to find that the insulin requirement was not increased, and that in some adults it was actually lowered. Geyelin used diets containing 2, 3 or more grams of carbohydrate per gram of fat. Meanwhile, Sansum, Blatherwick and Bowden had reported results with insulin cases on diets high in carbohydrate, which they had come to adopt for general reasons. These papers by Sansum et al and Geyelin have been followed by others here and abroad, such as those of Rabinowitch, Porges and Adlersburg and others, to which Dr. Geyelin may refer tonight, so that now in the insulin era we are in the midst of a "high carbohydrate" movement in which we discern an awakening on this side of the Atlantic, and a revival in England and Europe, of interest in a type of diet and a problem of mechanism that has held the attention of groups of writers more or less continuously for 60 years. And in the course of the movement we see the recurrence with variations of certain conceptions and possibly also some of the errors that have been discussed at great length in the pre-insulin era. However, now we are better equipped than earlier writers to solve the theoretical and practical problem.

Mechanism of High Carbohydrate Diets. As stated above, the idea that led Dr. Geyelin to adopt high carbohydrate rations for children was that his diets had been too high in fat. As he is here tonight, he will correct me if I misrepresent him in stating that what he was after was low fat diets, and that in lowering the fat while keeping the calories and protein about the same, he necessarily

raised the carbohydrate. Then, having obtained his striking results, he interpreted them as due in part, at least to the positive action of carbohydrate.

The influence of the same conception concerning the injuriousness of fat is evident in the interesting experimental study of Dr. Russell Richardson of this city. Working with patients on diets of the high fat type but of moderate calorie magnitude, he kept the urine free of sugar and the blood sugar percentage within normal limits with certain fixed doses of insulin. He was then able to remove from a diet a given weight of fat and add the same *weight* of carbohydrate without changing the dose of insulin or causing glycosuria or hyperglycemia. Thus in one case the diet provided C.57, P.58, F.150, Cal.1930. The insulin dose was 46 units, the blood and urine were normal and the patient was free of insulin reactions. The fat was then lowered by 93 gm. and the carbohydrate increased by 93 gm. so that the diet provided C.150, P.58, F.57, Cal.1345. With the insulin dosage remaining the same, the blood and urine remained as before. He found that such changes could be made all at one time with patients who had been somewhat undernourished. With obese patients the experiment failed, sugar appearing in the urine when the change was made. Richardson says "There is apparently present in these patients the *influence of the body fat* which makes it impossible for them to take advantage of *the reduction of fat in the body*" and further "We feel that the ability of patients to metabolize more carbohydrate can not be due to increased tolerance for food (glucose)—No time was allowed for development of a great tolerance—The patients were also on the highest diet which they could take with the given amount of insulin—In the insulin patients if the insulin had been sufficient to allow for a marked increase in carbohydrate, it would have been sufficient to cause shock during the period of the low-carbohydrate high-fat diet." He suggests a reciprocal relation between the fat and the carbohydrate metabolism.

Now it must be said of these experiments that three changes are made simultaneously — lowering of the fat and total calories and raising of the quantity of carbohydrate. There is little question that in undernourished or even normally nourished patients who have been living on diets absolutely too low in carbohydrate it may be possible to obtain results similar in kind to those obtained by Richardson simply by adding carbohydrate, as has already been shown. Nevertheless it may be recalled that carbohydrate is convertible in the body into fat and that fat may be burned directly as such. Indeed under suitable physiological conditions a major fraction of all the utilizable carbohydrate that enters the body may be oxidized indirectly by primary reduction to fat, a two stage process in which the total quantity of oxygen consumed and the total quantity of carbon dioxide produced are the same in the end as they would be if the sugar were burned directly. Therefore, what we refer to as a patient's tolerance for carbohydrate depends not alone on his ability to oxidize sugar directly, but in a very considerable measure on his ability to burn it indirectly, that is to say—by primary conversion into fat and ultimate burning of the fat. Even if we granted the theoretical contention of some writers that fat may be changed into carbohydrate, the above statement would hold. The question may be raised as to the possible limits of fat formation from carbohydrate, and as to the relative availability of this method of sugar disposition in a fat as compared with a lean individual. As the fat reservoirs of the body fill up and the body approaches fat saturation, then, other factors remaining the same, might we not expect a slowing down of the rate of conversion of carbohydrate into fat, and a corresponding impairment of the carbohydrate tolerance? Perhaps this is what Richardson had in mind, and if so I believe that he offers a plausible theory of how too much fat in the body may lower the tolerance for carbohydrate. However, in the case of a patient who is already spare and undernourished, it would seem to me doubtful whether the removal of fat from the diet would serve the same pur-

pose. In such cases it would seem necessary to attribute any increase of the tolerance for carbohydrate to the positive action of carbohydrate itself, or to be very cautious—something contained in carbohydrate foods. The mechanism of the positive action of carbohydrate food remains problematic.

Practical Adjustment of the Proportions of Carbohydrate and Fat. If in the case of a given patient weighing 60 kg. general requirements had been fairly fulfilled by a diet containing 1800 calories, 240 of which were provided by 60 gm. protein, leaving 1560 non-protein calories, and if the carbohydrate amounted to 60 gm. and the fat to 146 gm. the diet would be of a relatively high fat type, and the question would rise as to whether conditions would be improved by the addition of carbohydrate and the subtraction of fat. One might then remove say 10 gm. of fat, add the calorie equivalent or 22.5 gm. of carbohydrate, observe results, and if they were desirable, repeat the process. If after 2 to 3 or 4 steps the insulin requirement were found to rise, one might stop or reverse the procedure. Or, if, after the carbohydrate had risen to 140 to 150 gm. and the fat had fallen to 85 to 80 gm. the patient felt that he was not receiving enough fat foods such as butter, cream or oil to make his menus agreeable to him, one might stop for no better reason than that. In a number of our cases in which we have followed roughly such a procedure, there have been definite advantages in raising the carbohydrate to levels between 2 and 3 gm. per kg. of body weight. I have not been struck by additional advantages resulting from further elevation of the carbohydrate using as criteria the insulin requirement per *calorie* of diet, frequency of reactions and the comfort of the patient. In some cases conditions have been less satisfactory on diets too high in carbohydrate. I have had but a limited experience with very high carbohydrate diets, and shall listen with interest to Dr. Geyelin. It has seemed to me that the most effective diet would be one on which the patient would obtain the necessary number of *calories* on the lowest possible insulin dose.

DIABETES IN CHILDREN*

Priscilla White
Boston

The problems of those who care for the diabetic child of today are largely five:—(1) the treatment of the uncomplicated case; (2) the prevention and treatment of the direct and indirect complications of the disease; (3) the control of emergencies which, in a few hours, can convert a controlled into an uncontrolled case; (4) the protection of the individual child; and (5) the prevention of the transmission of the disease.

The direct complications of diabetes are obviously coma and hypoglycemia; the indirect complications are the end results of uncontrolled diabetes. In the order of the frequency with which they have occurred in the series of 900 juvenile patients who have come under Dr. Joslin's care from 1898 to 1933 they are pseudo-dwarfism, arteriosclerosis, cataracts, infections of the skin, and xanthoma. The emergencies which can convert the controlled into an uncontrolled case are surgical complications, acute or chronic infections.

The treatment of the uncomplicated juvenile case is the most frequent problem. It is more involved than that of adult diabetes because it consists of two phases, initial adjustment and periodic readjustment to allow for growth and development. Furthermore, one must contend with the greater physiological and emotional instability of the child. The actual principles of treatment employed in juvenile and adult diabetes are the same, diet, insulin and exercise. In the process of desugarization we still employ undernutrition prescribing for the child's initial diet 100 grams of carbohydrate, 1 gram of protein per kilogram of body weight and enough fat to yield 30 calories per kilogram. The diet is increased daily until the desired diet

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* Delivered before the joint meeting of The New York Academy of Medicine and the Medical Society of the County of New York, October 30, 1933.

for age and size of the child is attained. Prolonged observation of cases under immediate control and with normal activity has demonstrated to our own satisfaction that the following diets permitted an average gain of from one-half to three-quarters pounds a month and fulfilled our own standards for controlled diabetes namely, that the level of the sugar of the blood should be below 200 mgs., glycosuria less than 10 grams in 24 hours and the cholesterol content of the blood normal, 230 mgs.

			Average diet in grams			
Age Yrs.	Cals./kg.	P./kg.	C.	P.	F.	Cals.
5	75	3.0	140	60	70	1400
10	65	2.5	160	70	80	1600
15	45	1.5	180	85	90	1900

We still limit the carbohydrate to 200, the protein to 100 and the fat to 110 and divide the carbohydrate one-fifth for breakfast, two-fifths at noon and at night.

A caloric increase of 5 or 10 per cent is made every six months or year according to the needs of the individual child so that he may grow two inches in height and six pounds in weight annually during childhood and double this amount during adolescence.

Insulin, to juvenile patients, is given continuously from the day of diagnosis and is considered the variable in treatment whereas the diet is the relative constant. We give the maximum dose one hour before breakfast, a slightly smaller dose one-half hour before the evening meal and, after the third year of diabetes, a few units at 10 o'clock or midnight. Sometimes an even distribution every 8 hours is more efficient or the administration of insulin before each meal with or without the late night dose.

Rearrangements of carbohydrate during the three major meals or in accessory lunches, readjustments of insulin and exercise are made according to qualitative four period tests, the level of the fasting blood sugar or one taken at eleven o'clock in the morning, four o'clock in the afternoon or an hour after a meal. There can be no pattern of

treatment applicable for all cases. There can be no constant pattern for the same patient day in and day out for the regimen of the individual day governs the diabetic schedule.

The prevention of both the direct and indirect complications of diabetes constitutes half of the diabetic problem of today. The direct complications coma and hypoglycemia command the attention of those who treat juvenile diabetes because they occur more frequently in the child than they do in the adult patient. The indirect complications, the degenerative changes, command attention even more imperatively for they are more tragic when they occur in youth. They must be checked all the more vigorously because of the evidence that decreasing severity of diabetes occurs when young patients have attained full growth and development.

Coma, no longer the inevitable lethal factor of juvenile diabetics, occurs frequently, too frequently. Only 1 in 100 of our adult patients has had coma whereas 1 in 10 of our juvenile patients has recovered from one or more attacks. The reasons for this greater frequency are the acute onset of diabetes in childhood so that the first hint of the existence of the disease may occur during severe acidosis or coma and greater susceptibility to minor systemic infections, as well as more frequent dietary indiscretions. In spite of the greater frequency the prognosis for recovery in the younger patient is better. Since 1923 only one death has occurred in 97 successive juvenile admissions at the New England Deaconess Hospital. Other hospitals have an equally good record. Coma, however, cannot be passed over lightly since it is still the major cause of deaths in those children who die outside the hospitals. The cardinal signs and symptoms are invariably present but the nausea and vomiting followed by leucocytosis and abdominal pain simulate an acute surgical abdomen, the Kussmaul breathing, pneumonia so that the primary cause, acidosis, is over-looked, being unrecognized it is untreated and the child who should recover dies.

The treatment of coma in the child differs little from the treatment of coma in the adult. Insulin early and in repeated doses, the amount depending upon the size and age of the patient and the duration of the diabetes as well as the clinical severity of the coma. From 5 to 40 units are given every 15 minutes for two hours then hourly until clinical improvement is evident. Actually from 30 to over 600 units have been given in twenty-four hours. Fluid is used to combat dehydration, from 500 to 6000 c.c. of normal salt solution in the first twenty-four hours. Gastric lavage and enemata are employed to combat lack of gastro-intestinal tone. Adrenaline may be used to combat circulatory failure which, however, seldom occurs in childhood. Glucose may be resorted to if renal block is imminent and carbohydrate given up to 100 grams by mouth in the first twenty-four hours.

Hypoglycemia, caused by irregularities of insulin, diet and exercise, like coma can generally be prevented by intelligent anticipation. There is always one factor to contend with—failure of absorption of food after the administration of insulin. In the child beside the usual symptoms the quiet child and the child in tantrums must be considered hypoglycemic until otherwise proved.

The treatment of the condition is self evident, replacement of carbohydrate by mouth if the patient is conscious, by vein or under the skin if the patient is unconscious. To the unconscious patient we prefer to give a 50 per cent glucose solution intravenously. This not only replaces the needed carbohydrate quickly but tends to combat the cerebral edema which occurs in severe cases of insulin shock.

Of the indirect complications of diabetes pseudo-dwarfism is the most frequent, the easiest to prevent and to remedy. The condition is a newly recognized one. A survey of the past histories of these patients shows that dwarfism has a single cause—undernutrition. This may be produced in a variety of ways but mainly one of four. It may be the result of undernutrition treatment of the

pre-insulin era. For this the physician is blameless. One-half of the 54 pseudo-dwarfs in our own series were survivors of the pre-insulin era.

It occurs in the insulin era among those patients treated for periods of time without insulin and where the diet is persistently reduced to bring about sugar freedom. The most difficult lesson to teach parents of diabetic children is the following. When the child grows he requires more food and more insulin. In our own patients the dosage of insulin has doubled from infancy to 15 years of age practically regardless of the duration of the disease. Any increase in insulin dosage indicates to the parents that the disease has become progressively worse and they will resort to all sorts of measures to reduce the dosage of insulin or at least to maintain it at the same level, actually placing a child of 12 upon a diet calorically inadequate for an infant of one.

It occurs furthermore, in some children whose disease is uncontrolled because of diet breaking. This is mostly among the younger children for they commit dietary indiscretions secretly and the dosage of insulin is not changed. The older children have become very adept at balancing diet and insulin under the same circumstances.

The onset of the condition is insidious because at the commencement of diabetes the child is on the average two inches above the standard height for age. It would therefore take three years of complete cessation of growth before the condition became apparent. These children grow a little, at the rate of 0.5 inches a year, therefore it is not until the fifth year of diabetes that the retardation is evident. This merely emphasizes the importance of checking annual rates of growth in diabetes as well as deviations from standards.

The treatment of dwarfism consists of high caloric diet to counterbalance the high energy requirement. The basal metabolism rate of these pseudo-dwarfs was plus 18 compared with plus 11 for all diabetic children and plus 2 for tall diabetic children.

Arteriosclerosis is the next complication in order of its frequency. It has been recognized in 33 of our juvenile patients. It is a rarity in young persons as shown by our own control group and by a review of the literature in which Pearl Zeek could find the records of only 98 cases in non-diabetics covering a period of 100 years. The common causes, nephritis, lues and sepsis, have not occurred in our own cases. The two abnormal conditions which occur in diabetes are alterations of fat and of carbohydrate metabolism. In a comparison of our cases we could find little clinical correlation between arteriosclerosis and high blood sugars in children, but arteriosclerosis occurred fifteen times more frequently in the group with high blood cholesterols. In the acidosis of uncontrolled diabetes the conditions are right for the redistribution of calcium from bone, union with cholesterol esters which are unsaturated fats and final deposition in the blood vessels and in the lens of the eye. Therefore, our standards for the control of diabetes are blood sugars below 200 milligrams and cholesterol below 230 milligrams.

Cataracts have been recognized in twenty-one of the group. Here again we have found a positive correlation between abnormality of cholesterol metabolism and frequency of cataracts, but our series is too small to be conclusive.

The tragic devastation of abnormal fat metabolism in juvenile diabetes is illustrated in a patient, Case No. 4568, who developed diabetes at 12 years of age in 1922. At no time has her diabetes been under control. From 1929 to 1933 the cholesterol varied from 500 to 300 milligrams. In 1924 x-ray examination of the legs was negative. From 1929 to 1933 she had xanthoma diabeticorum, frequent attacks of acidosis, carbuncles and abscesses. In September, 1933 she returned to the clinic nearly blind—and hopelessly so because of retinitis proliferans and with well marked [illegible] els of the legs.

Failures in the treatment of the young diabetic of today are not due to the type of treatment employed but to the lack of treatment or uncontrolled disease. This we consider hopeful but control of diabetes depends upon the patient—an unfortunate situation in childhood since the child lacks wisdom, therefore infinite tact, patience and understanding must be applied to the individual child and his problems.

Almost any degree of abnormal health in the juvenile patient must be considered an emergency, because it is slight deviations from normal which precipitate acidosis and coma even in a fairly well controlled case in as short an interval as twelve or twenty-four hours. Therefore parents and patients besides being taught to notify the family physician immediately in case of illness must be taught simple rules for the management of days of illness. These are the same as our own for pre- and post-operative treatment. Insulin every two, four or six hours depending upon the degree of reduction with the Benedict test. The child of fifteen—15 units if red or orange, 10 if yellow, 5 if yellow green, to the child of ten—10 units if red or orange, 5 if yellow or yellow green—to the child of five—5 units if red or orange, 3 if yellow. The diet should be reduced to from 100 to 150 grams of carbohydrate and a negligible amount of protein and fat. Such a diet could be one and one-half or two and a half quarts of milk.

In any discussion of the care of the diabetic child the inheritance of the disease must appear for it is this particular generation which must be taught to safeguard the next. It was the child in fact, who first convinced us of the importance of inheritance, revealed its latency, and suggested the mode of transmission.

We are dealing with a complicated problem. Obvious inheritable conditions are evident at birth or in early childhood. This is not the case with diabetes, few patients developing the disease in early life and the majority in middle or late life. Therefore it cannot be inheritance alone but

inheritance plus some other factor in the internal or external environment which permits the expression of the disease. Furthermore, with the exception of the mating of diabetic and diabetic we have to start an analysis such as ours backward since the only way we can identify an individual as a carrier of a disease is by the fact that he has produced an offspring with the disease. Increasing duration of diabetes tends to reveal the carrier history for among diabetic children 1 in 5 has a diabetic relative when first seen, 1 in 3 after five years and every other one after ten years.

The conclusion that diabetes is inherited as a Mendelian recessive is based on (1) the finding of a greater evidence of diabetes in a diabetic than in a control population selected at random; (2) the demonstration that the Mendelian law applied to a large series of case histories selected at random; (3) the check on the case history method by the direct examination of the blood and urine of a small series of families, diabetic and control, not selected at random but selected so that we have an even distribution of families in the three types of Mendelian population.

The statistically significant difference between the occurrence in a diabetic and control population was this. In the diabetic population 8 per cent had parents with the disease, in the control population 2 per cent. Diabetes occurred ten times more frequently in the brothers and sisters of the diabetics than it did in the control population.

When we applied the Mendelian hypothesis to our case histories, from the statement above, it was evident that we would have to keep to the recessive side of the pattern. If diabetes were inherited through a simple dominant gene one would expect more instances of parental disease.

Mendelian expectations on a recessive basis were fulfilled when we based our analysis upon two facts—age incidence and survivorship. The age incidence factor is

this. In each consecutive thousand of our own cases the same number have age of onset in the first decade, in the second decade, etc.—our clinic, other American clinics, European clinics.

The survivorship factor is this. Persons predestined to the disease live and die at the same rate as those not predestined. Thus the predestined diabetic can contract tuberculosis and typhoid fever and die of these conditions or be killed in an automobile accident just as a person not predestined. From this a prediction curve can be constructed. This represents the incidence of diabetes in a diabetic population and lies slightly below the age at onset tables which appear in the standard text book. This analysis was done by Dr. Pincus at the Department of Physiology at Harvard University and a preliminary report has already been published by Dr. Pincus and myself in the American Journal of Medical Sciences.

Although the result of this work seemed convincing it was obvious that, dependent upon case histories, patients might be incorrectly classified either as diabetic or non-diabetic and early or latent cases unrecognized. The third part of the study answered this objection, since it confirmed case histories in most instances and although it revealed latent cases they occurred where we expected them and did not alter our results. Among the cases tested most severely—by tolerance test—were 87 members of diabetic families and 52 controls. Eight hyperglycemic curves were found—all in the diabetic families. Four other abnormal curves were found all save one in the families of diabetic individuals.

If the 10 per cent increase is incorporated it altered the type of cross once—an unidentified diabetic parent was recognized. It brought one family into the series revealing a child with the disease. It revealed one sibling in the carrier x carrier cross, two in the diabetic x carrier cross and two in the diabetic x diabetic cross.

The analysis furthermore proved the crucial test of the theory which rests with the mating of diabetic and diabetic. Twenty-three such families were studied. It is the crucial test because, first this is the only group in which the identity of the parents is stabilized. They are all diabetic and will remain so and second all the children of two diabetics should eventually develop the disease. If our hypothesis has been correct we should not only have predicted the number of diabetics in the children of our twenty-three conjugal families but also the age at onset on our prediction curve. We expected 14 of the 109 children to be diabetic—16 clinical cases were found and two others had hyperglycemia. Furthermore in most instances, in fact 6 out of 8 decades, the number expected in each decade appeared in accordance with the prediction curve.

Our hypothesis holds. What does this mean? It means first that we have a relatively small group upon which to concentrate for the second etiological factor and second that the control of diabetes is possible. For if a diabetic marries a diabetic all the children are predestined diabetics but only 0.2 per cent will develop it in the first decade, 3 per cent in the second, 5 per cent in the third, 10 per cent in the fourth, 20 per cent in the fifth, 30 per cent in the sixth, 50 per cent in the seventh, 60 per cent in the eighth. If a diabetic marries a carrier one-half are predestined to diabetes. (One-half the prediction curve.) If a carrier marries a carrier one-fourth are predestined to diabetes (one-quarter of the prediction curve) but if a diabetic marries a pure non-diabetic none of the children are predestined.

But not only must we train our diabetic children to marry into pure non-diabetic families but we must also carry this teaching to the children of diabetics for they represent true and insidious carriers of the disease.

Five points I wish to re-emphasize. Deaths from coma and hypoglycemia even their occurrence are needless today. Pseudo-dwarfism is insidious of onset, results from under-

nutrition even in the insulin era, but should never occur. Degenerative complications, arteriosclerosis and cataracts are found even in childhood but only when the disease is uncontrolled. There appears to be a positive correlation between abnormal fat metabolism and degenerative changes; and last, the capacity for developing diabetes is transmitted as a simple Mendelian recessive trait.

1. Zeek, Pearl, *Arch. Path.*, 1930, *10*, 417.

2. Pincus, Gregory and White, Priscilla, *Am. Jl. Med. Sci.*, 1933, *186*, 1.

CONSIDERATIONS BEARING ON THE SUCCESSFUL TREATMENT OF DIABETES MELLITUS*

James Ralph Scott

The cause of diabetes is unknown. Its successful treatment therefore, in the present state of our knowledge, depends first upon a consideration of the various factors that are known to contribute to its onset. There are several of these contributory factors. Perhaps the most important are:

1. *Obesity.* Obesity certainly is a factor in diabetic deaths, for Dublin has shown that extreme overweights have a mortality eight and a half times in excess of normal weights, and thirteen times the rate shown in underweights—he is speaking here of diabetic deaths only. Rabinowitch, of the Montreal General Hospital, states it tersely when he says, "When a man adds 10 pounds to his belt line, he subtracts one year from his life line." Certainly, treatment of diabetes to be successful must stress the importance of overweight as a predisposing cause.

2. *Heredity* appears to be a factor in the incidence of the disease. Recent investigations—and particularly a scholarly piece of work published three months ago by White and Pincus, of Boston—strongly suggest that diabetes may be inherited as a Mendelian recessive trait. If this be so, it gives hope to the diabetic patient who wishes to marry and have children, provided the marriage be to a non-diabetic person. Conversely, marriage of two diabetic persons would be sure to produce diabetic children, and should be avoided. The prevalence of diabetes among Jews as a race is probably an hereditary phenomenon.

3. *Age and Sex* are factors influencing the incidence of diabetes. The greatest mortality from diabetes occurs in the 5th and 6th decades of life in both sexes. Moreover,

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the death rate among women is rising much more rapidly than that among men until now, in this age group, more than twice as many women as men die of the disease. Apparently after middle age something happens to women that does not happen to men to account for this increasing mortality. Dr. Mosenthal rightly stresses the importance of pregnancy as a contributing factor, for it is definitely known that pregnancy diminishes the glucose tolerance in diabetic women for a considerable period of time, and possibly permanently. That the incidence of diabetes among married women and widows is greater than among single women also supports this thesis.

4. *Endocrine imbalance* may be a contributing factor in the onset of diabetes. We know that in the presence of hyperthyroidism for example diabetic patients show an insulin resistance. Diabetic girls develop a diminishing glucose tolerance at the onset of menstruation. Recent animal experiments show that in de-pancreatized dogs fatal diabetes can be prevented by the removal of the hypophysis.

In an appreciable number of human autopsies done on patients dying of diabetes, no destruction of the islands of Langerhans can be demonstrated. All these facts suggest that diabetes is something more than a disease of the pancreas alone, and it may be that further research in this fertile field will reveal the actual, immediate cause of the disease.

5. *Psychic or nervous shocks* have been thought to be contributory causes of diabetes. It has been proved that emotional stress affects the glucose metabolism even in normal persons, and we know it diminishes the glucose tolerance in diabetics. It may be that the stress and strain of modern, urban civilization is a factor in the increasing incidence of diabetes. Two facts supporting this thesis are, first that diabetes is more prevalent in the city than in the country, and second, that the death rate from diabetes among negroes in our northern cities is twice that of the same race in the South.

6. *The changing dietary and living habits* of our people may be a factor in the increasing prevalence of diabetes. A diet consisting mostly of cereals, fruit, vegetables and dairy products has replaced one in which meat predominated. The per capita consumption of sugar has increased over 300 per cent in the past 60 years. At the same time there has been a mass migration from the country to the city, and the number of manual laborers has diminished. This is significant, for in all mortality tables classified according to occupation laborers have the lowest place.

While this brief review of some of the factors which appear to influence the incidence of diabetes does not solve the problem, it is hoped that a further study of them may throw some light on the essential nature of the disease, and will have a bearing on its successful treatment.

In the actual application of our knowledge to the treatment of the patient, the most important consideration of all is the *education of the patient* in the management of his own case. One has only to check over one's own list of patients to realize that those who show the best results are the ones who know the most about their disease. Every diabetic patient should know how to do three things—

1. Test his urine for sugar.
2. Calculate his diet (by weight or measurement).
3. Give himself insulin.

Moreover, he should learn that the criteria of successful treatment are—

1. A sugar free urine.
2. A normal blood sugar.
3. A weight within 10 per cent below the normal for age, height and sex.

All except the mildest cases should be placed on a weighed diet from the start. At first the urine should be tested four times daily, before breakfast, and one hour after each meal. Insulin is given according to these tests,

and can be increased or decreased to meet the patient's requirements. A blood sugar determination should be done at least once a month. As the patient's knowledge of his disease improves, this regime may be modified at the discretion of the physician.

The protein requirements of adults should be one gram per kilogram of body weight, and that of children from 1.5 to 3 grams per kilo. A fastidious calculation of the theoretical caloric needs of the patient is unnecessary. After the protein requirement is calculated, the caloric content of the diet can be obtained by giving enough carbohydrate and fat to maintain the patient at his ideal weight, *always* giving more carbohydrate than fat.

A good diet to start on, and one which I use on both private and ward patients, is C 120, P 65, F 50—1190 cal. Any other diet would do just as well. The point is that each physician should decide on a reasonable diet that satisfies his particular idiosyncrasies, and then increase or decrease it depending upon whether he wants the patient to gain or lose weight. *The patient's weight is the best guide to his caloric requirements, and his four daily urine tests are the best guide to his insulin requirements.*

Some time ago I decided to chart the course of a patient who has been under my care for 7 years. She is single, a school-teacher, and a severe diabetic, making it necessary to weigh every gram she eats. She works hard, goes to the theatre, swims in the summer and does everything her associates do. Her weight is normal. Much to my surprise, I found that for the past two and a half years she had been doing all this on a diet of 950 calories—C 120, P 50, F 30. Fortunately I had not been feeding this patient on the basis of her theoretical caloric requirements, for if I had, she would have been the victim of obesity by this time. To guard against any possible Vitamine A deficiency in this low fat diet, she takes one capsule of Haliver oil daily, which appears to supply her needs.

I should like to close with a warning against giving too much insulin to our older diabetic patients. Nathanson, of the University of Minnesota, showed by autopsies on 100 diabetics that "the incidence of *coronary sclerosis* is approximately six and a half times greater in diabetics than in non-diabetics". This is a very significant finding, for we know that the coronary heart muscle needs more glucose to function properly than the normal heart muscle does. Therefore, *if* coronary sclerosis is more common among diabetics, and *if* a low blood sugar is harmful to these damaged heart muscles, the safest course to pursue is to treat all diabetic persons over 50 years of age as potential heart cases, and to maintain an adequate blood sugar level at all times. Consequently, I have adopted as a normal blood sugar for patients in this group 150 mg. per 100 c.c. of blood.

In the time allotted I have been able only to touch upon a few of the general considerations bearing on the treatment of diabetes. A detailed account of the more important phases of treatment is given by my colleagues on this program.

TREATMENT OF DIABETIC COMA*

HERMAN O. MOSENTHAL

The principles guiding therapy in diabetic coma have changed completely during the last decade. Ten years ago, acidosis was the synonym for diabetic coma accepted by the clinician. At that time, the main effort at controlling this disturbance, which was usually fatal, was the administration of bicarbonate of soda in large amounts, by mouth, vein, rectum and hypodermoclysis. This was done for the purpose of forcing the elimination of accumulated acid by way of the kidneys and providing adequate bases for internal respiration. Bicarbonate of soda is just as useful today in this regard as it was ten years ago, but it has become unnecessary since diabetic coma is no longer treated as an acidosis but as a diminished power of the body to assimilate glucose.

Insulin, perfected by Banting, Best and the Toronto group of scientists, has enabled physicians to manage diabetic coma, not as a poisoning by acid, but as an intoxication due to the marked impairment of the ability of the tissues to utilize glucose. This principle was appreciated long ago but it could not be applied because, without insulin, clinicians could not light the fire of the carbohydrates in which the fats must be consumed. This can be accomplished now, so successfully that most cases can be revived within a few hours.

The most important point in the successful treatment of diabetic coma is the proper use of insulin; this matter will be taken up first and the remaining parts of the treatment subsequently.

The early treatment of this condition is very essential. Diabetic patients should be instructed that if they have an infection, if they become subject to nausea or vomiting,

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if their respiration becomes deeper than usual, or if they feel out of sorts in any way, they should inform their physician immediately.

Insulin should be administered in comparatively small doses and at frequent intervals. In this way, more carbohydrates are digested per unit of insulin than with a single large dose; a huge amount of insulin at one time—100 to 400 units as have been given—may result in hypoglycemic reactions for many hours subsequently; this is a real danger which has to be guarded against; it is worth remembering that more insulin can be given with an almost instantaneous effect on the carbohydrate metabolism, but insulin cannot be removed from the body, nor can extremely large doses be readily compensated for by the ingestion and intravenous injection of glucose. The first dose of insulin should be given partly by vein to insure immediate results, and partly subcutaneously so as to prolong its action; 20 units by vein and 20 units subcutaneously is usually sufficient.

After this initial treatment, insulin in doses of 10 to 20 units should be given subcutaneously every hour or two hours. The amount and the frequency of the doses are regulated in the first place according to two signs: the depth of the respiration is a good measure of the persistence and intensity of the acidosis; another criterion of the effect of insulin upon the coma, naturally, is the degree of recovery from the unconscious state.

In the second place, the result produced by the insulin should be judged by an hourly or two-hourly careful examination of the urine. This should be obtained by catheter if necessary. The urine is examined for sugar and for diacetic acid. If glucose persists in the urine in appreciable quantities, the hourly or two-hourly subcutaneous injection of insulin is continued. When sugar is present in the urine in only small amounts and there is need for further insulin effect, then glucose must be given by mouth, vein or subcutaneously in order to furnish the injected in-

sulin, sugar upon which it can act. The subject of the administration of glucose in diabetic coma will be taken up in greater detail later on.

The presence of diacetic acid in any specimen of urine as shown by the ferric chloride test, calls for the utilization of more glucose and consequently the continued use of insulin. The same is true of the persistence of the physical signs of coma, namely, unconsciousness and the deep breathing.

The careful and painstaking procedure according to this outline usually results in the recovery of consciousness within a few hours.

The equipment necessary for this treatment should be kept in readiness by every physician. It consists of two four-ounce bottles—one of Benedict's solution and one of ferric chloride solution of 10 per cent or stronger—four test tubes preferably of pyrex glass so that they will not break on heating, one alcohol lamp, 400 units of insulin, and a hypodermic syringe. This is all that is absolutely essential for emergency use.

The determinations of blood sugar and the CO_2 combining power of the blood, are exceedingly valuable and comforting determinations for the guidance of treatment. However, they are not absolutely necessary. Furthermore, unless the patient is in a hospital with adjacent and functioning laboratories, the reports would come in too slowly to be of much help. Decisions must be made regarding the regulation of insulin and glucose every hour or two, and the results of laboratory tests that are reported late during these intervals, are past history and not of great value for the control of the immediate handling of the situation.

Although it interrupts the flow of thought, I should like to call attention here to a matter which Dr. Bolduan of the Department of Health in New York City, called to my attention. Dr. Bolduan sent out questionnaires regarding the diagnosis and treatment of cases of diabetic coma

which terminated fatally. Many of the answers indicated that the patients had succumbed to diabetic coma without receiving insulin. According to the answers given, this astounding fact apparently is not the error of the physicians, but is due to the unwillingness of patients or their families to submit to insulin therapy. Why there should be this deep-seated objection to the life-saving benefits of insulin, it is difficult to understand. However, from these questionnaires it becomes perfectly evident that the education of diabetic patients and their families must be carried out more effectively. The same antagonism to the use of insulin is being encountered as there has been to other life-saving measures such as vaccination and diphtheria antitoxin.

When the urine becomes free of diacetic acid, the patient returns to consciousness and the breathing is no longer deeper than normal, then insulin may be given three or four times a day and an appropriate diabetic diet resumed.

While the insulin brings about the adequate utilization of glucose, and through this, the complete oxidation of fatty acids and does away with the acidosis and coma, there are certain urgent effects of the inability to assimilate glucose in the comatose patient that must be taken care of. Some patients never recover consciousness although they are relieved of the acidosis, and others succumb after the coma is set aside, to the ravages which the diabetes and acidosis have imposed upon them. Such complications are attributed principally to dehydration. The dehydration comes about in diabetes largely through the polyuria incident to the elimination of glucose, and to the loss of basic material accompanying the excretion of excessive quantity of acids in the urine. Marked dehydration results in a rapid pulse rate, low blood pressure, impaired cardiac power, diminished surface temperature, oliguria and constipation.

Great care must be taken to meet these complications so as to prevent a fatal issue which may occur even though the coma itself has been overcome.

Every patient should be kept as warm as possible by the usual methods. Fluids should be administered in good quantities by mouth, subcutaneously or intravenously; possibly all three methods may be employed. At times there is vomiting or gastric distention. In this event the stomach may have to be washed out and only the intravenous and subcutaneous routes used for the administration of fluid. The fluid should consist of saline solution, according to the precepts given by Peters and his coworkers, to aid in the restoration of the proper acid-base equilibrium of the body and also to favor the retention of fluid.

There is some controversy as to whether glucose should be routinely administered, or not. It has been my belief that glycosuria favors polyuria and therefore there is a loss of fluid to the body when sugar is present in the urine. Furthermore, it would seem entirely superfluous to add glucose when the quantity of insulin administered to the patient has not succeeded in utilizing the excess of sugar which already exists within the body. Consequently, our patients have been given glucose only when the urine showed a low concentration of sugar, approximately less than 0.5 per cent, and when further immediate administration of insulin was indicated. This method of balancing insulin and glucose has proved to be satisfactory.

For the cardio-vascular involvement, we have resorted to digitalis with the idea of digitalizing the patient within 24 to 48 hours. When insulin was first employed in the treatment of diabetic coma, it was our experience that some of the cases succumbed to pneumonia after the coma had been set aside. The impression was gained that this was the result of pulmonary congestion existing during the period of unconsciousness. Since digitalis has been resorted to, the pneumonic complication has been absent. The rapid pulse rate, the low blood pressure are nearly always present in diabetic coma and are ample evidence of the need for cardio-vascular stimulation.

If rapid response is not obtained after the first rush of activity in caring for these patients is over, it is necessary to think of possible complications, as the presence of infection, an over-active thyroid, apoplexy. Such co-existing diseases have to be met on their own grounds and given due attention.

The treatment of diabetic coma has, through the availability of insulin, become one of the most simple and direct therapeutic problems in medicine. It is exacting in its demands upon the physician, the nurse and the patient, but the splendid results amply reward the effort.

FELLOW, MEMBERS AND ASSOCIATE ELECTED
MAY 3, 1934

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Associate:

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THE TREATMENT OF DIABETES WITH DIETS NORMAL IN CARBOHYDRATE AND LOW IN FAT*

H. Rawle Geyelin

In October, 1925 before the Section on Diseases of Children of the Pennsylvania State Medical Society, we reported the effects of feeding normal diets to insulin treated diabetic patients. This report was extended by further observations during the last eight years and a more extensive summary of our findings and conclusions on a much larger group of patients was reported before the American College of Physicians in February, 1933. In these two previous reports we emphasized the fact that each unit of insulin was capable of oxidizing more grams of carbohydrate when the patients were fed on diets in which the amount of carbohydrate, protein and fat approximated the proportionate and actual amounts of these foods as found in normal diets than when the older routine diabetic diets containing a preponderance of fat were given. These findings have been corroborated by Sansum and Rabinowitch and many other observers during the past eight years.

The purpose of the present communication is to emphasize certain effects upon the clinical course of diabetes which we have noted following the exhibition of these normal diets in insulin treated cases of diabetes. First, we propose to present data demonstrating the disappearance of hypercholesterinemia following the administration of normal diets. For this purpose we have collected 40 cases of diabetes who had all been treated with insulin together with diets high in fat and low in carbohydrate and who were subsequently transferred to diets containing normal proportions of carbohydrate, protein and fat. Of these 40 patients, 26 showed cholesterol figures that were greater than normal after varying periods on high fat or

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low carbohydrate diets. The remaining 14 cases showed blood cholesterol figures that were within the normal range. All these patients had been receiving the low carbohydrate high fat type of diabetic diet for at least one year before the change to the normal type of diet was made. Four of the patients had been receiving a comparatively low carbohydrate high fat type of diabetic diet for 6 years or more before treatment with the normal carbohydrate diet was instituted.

As an illustration of the type of diets which were being fed to most of the patients prior to their transfer to the high carbohydrate diet, we may cite only 3 cases out of the group of 40. First, H. N., case G-2376, male, 18 years of age, who first presented himself for treatment June 4th, 1932. His diabetes was first discovered January, 1930 and his diet from that time until June 4th, 1932 had been approximately 80 grams carbohydrate—90 grams protein—210 grams fat. He was receiving insulin three times a day, the total insulin dosage being 83 units per day. With this diet and insulin dosage he was able to remain free from sugar and also free from insulin reaction. At the time of his first visit his blood sugar was .247 per cent and his blood cholesterol .279 per cent and a trace of sugar was found in his urine. The diet was changed immediately to 325 grams carbohydrate—90 grams protein—80 grams fat and he was able to continue sugar free for the next year on a dose of insulin which never exceeded 52 units per day and which sometimes went as low as 42 units per day. His blood cholesterol has dropped to below .200 per cent and it has remained at this level continuously up to the present time. During this period the patient has gained 6 pounds in weight and ¾ inch in height. He has had no insulin reactions and his sense of well being is greatly improved. He insists that he has much greater physical endurance.

H. G., case G-2373, male, 18 years of age, first came for treatment February 24th, 1932. Diabetes had existed for 9 years. During the last 6 years of this time patient had

been on a diet of 65 grams carbohydrate—80 grams protein—200 grams fat with steadily increasing insulin until during the year prior to his admission he was taking 60 units of insulin per day and showing constant glycosuria. His blood cholesterol at the time of his first visit was .389 per cent; his blood sugar was .247 per cent; his urine contained 4.4 per cent sugar. The number of grams of carbohydrate per unit insulin was 1.9. His weight was 118½ pounds with considerable edema. His diet was changed to 300 grams carbohydrate—85 grams protein—75 grams fat and it has been gradually increased to 425 grams carbohydrate—85 grams protein—75 grams fat during the past 18 months. His insulin requirements are now 45 units per day and have been since January, 1933. He is continuously sugar free and has gained 11 pounds in weight and ½ inch in height.

W. I., case G-2443, male, age 22 at the time of first visit on April 5th, 1933. Has had diabetes since April, 1932, and his diet has been 150 grams carbohydrate—120 grams protein—190 grams fat with 65 units of insulin per day. Says he has been sugar free for the past year. At his first visit his blood sugar was .125 per cent; his blood cholesterol was .368 per cent; his urine was sugar free. His diet was at once changed to 350 grams carbohydrate—120 grams protein—90 grams fat; his insulin was reduced to 52 units per day. On this diet and insulin dosage patient remained sugar free and within 5 days the blood cholesterol was reduced to .257 per cent. One month later it was .142 per cent. Patient has remained sugar free and at the present time—October 25th, 1933—he is on a diet of 375 grams carbohydrate—100 grams protein—90 grams fat. The insulin requirement is 45 units per day and he has remained steadily sugar free.

Similar reduction to normal of the blood cholesterol has ensued in all the 26 patients alluded to above after the transfer from a diet high in fat and low in carbohydrate to one with the normal relationship of carbohydrate to fat.

It seems appropriate at this point to explain what is meant by a normal diet. By direct experiment we have found with a small group of normal individuals and with all of the present group of diabetics, that when left to their own devices, these patients, including the normal group, eat diets which contain carbohydrate, protein and fat in approximately the proportion of 4-1-1. Not all of these diabetic patients have been permitted to eat as much carbohydrate in relation to fat as this. In many of our diets, for example, the relation of carbohydrate to fat has been approximately 3 or 3½ to 1. We have found, however, that there are a few patients whose blood cholesterol does not return to normal limits until the proportion of carbohydrate to fat in the diet has reached that of 4 to 1.

The length of time which we have found is necessary to reduce the blood cholesterol after these changes in diet have been instituted varies from 1 to 8 weeks but in most patients the reduction of pre-existing high blood cholesterol to normal occurs within 2 weeks. In one case we have conducted the following control experiment: a diabetic boy, M. H., case G-2152, 9 years of age at the time of his first visit on November 20th, 1929, was put on a normal diet with 16 units of insulin in the morning and 16 units at night and maintained on this diet 2 years. During this period of time his blood cholesterol was always within normal limits. In November, 1931 his diet was changed to 70 grams carbohydrate—90 grams protein—150 grams fat. This diet was maintained for 8 months, at the end of which time he had developed hypercholesterinemia. Incidentally, the amount of insulin which he required during this low carbohydrate period was equal to the amount which he had required when his blood cholesterol was within normal limits on the normal carbohydrate diet. In May, 1932 he was returned to the normal diet and within 3 weeks his blood cholesterol had again reached normal limits.

The second observation which we wish to emphasize is one which we have called attention to in previous com-

munications, namely, the increased effectiveness of insulin in the oxidation of carbohydrate which follows the administration of normal diets as compared with the effectiveness of insulin observed when patients have been on a low carbohydrate high fat diet. This effect has been noted in all cases and is striking. It is true that the increased effectiveness of insulin does not occur immediately in some few patients and in 4 patients was not striking until 6 months after the transfer from high fat to normal diet had taken place.

This increased effectiveness of insulin following the substitution of a normal diet for one relatively or absolutely high in fat is apparently a permanent effect. In 21 patients who comprise the original group of diabetics receiving this diet, there has been no appreciable loss of insulin effectiveness after 8 years of continuous administration of a normal diet.

Many children who had previously been on lower carbohydrate higher fat diets, had gained little or no weight and had not grown in height for 2 or 3 years have gained as much as 15 pounds in weight and 3 inches in height in one year. The gain in sense of well being, physical strength and endurance has been noted in nearly all the cases.

In conclusion, all patients who have received the normal or higher carbohydrate lower fat diet after a period of several years on the lower carbohydrate types of diet (with relative or absolute high fat) demonstrate the following facts:—

1—Hypercholesterinemia, where it has previously existed, is abolished.

2—Increased insulin effectiveness as judged by the number of grams of carbohydrate that each unit of insulin is capable of oxidizing.

3—Resumption of normal growth in weight and height.

4—Increase of physical well being, muscular strength and endurance.

W. I. CASE G-2443. MALE.

Date	COH	Pro.	Fat	Total COH	Calories	Insulin	Total Insulin	Urine Sugar	Blood Sugar	Blood Chol.	COH Grams per U. Ins.	Age	Wt.	Ht.
1932														
April (onset)	100	50	50	130	1050	4 units for 4 days, then stopped					32.5	21½	135	
Aug.	150	120	180 to 190	222	2745	25-25-15	65	sugar free			3.4			
1933														
April 5	350	120	90	422	2690	30-5-20	55	sugar free	.125%	.368%	7.5		145	5′10¾″
April 10	350	120	90	422	2690	28-0-14	42	sugar free	.115%	.257%	10		147	
May 8	350	120	90	422	2690	26-0-14	40	sugar free		.142%	10.5			

H. G. CASE G-2373. MALE.

Date	COH	Pro.	Fat	Total COH	Calories	Insulin	Total Insulin	Urine Sugar	Blood Sugar	Blood Chol.	COH Grams per U. Ins.	Age	Wt.	Ht.
1923 (onset) to 1932 (approx.)	65	80	200	113	2380	30-0-30	60				1.9	9		
1932														
Feb. 24	300	85	75	351	2095	35-5-25	65		.241%	.389%	5.4	18	118½	5′3⅞″
March 4	350	80	80	398		35-0-23	58		.179%	.222%	6.8		121	
June 22	400	85	80	451		30-0-20	50		.119%	.146%	9.0			
1933														
Feb. 6	425	85	80	476	2760	20-0-25	45		.125%	.189%	10.6		133½	5′4⅜″
June 21	425	85	80	476	2760	20-0-25	45		.101%	.195%	10.6		129⅛	5′4⅜″

H. N. CASE G-2376. MALE.

Date	COH	Pro.	Fat	Total COH	Insulin	Urine Sugar	Blood Sugar	Blood Chol.	COH Grams per U. Ins.	Age	Wt.	Ht.
1930												
Jan. (onset)										15½	98	
Oct.	50 to 100	90	180 to 250	124	83				1.5		106	
1932												
June 4	325	90	80	379	65	plus to plus minus	.247%	.269%	5.8	18	140	5′7″
June 9	325	90	80	379	65	minus	.259%	.200%				
Sept. 16	325	90	80	379	52	plus minus	.196%	.216%	7.2		139¾	5′7⅜″
Nov. 8	325	90	80	379	55	occ.	.156%	.191%	6.8		139⅛	5′7½″
1933												
Feb. 3	325 to 350	90	80	379 to 404	54	plus to plus minus	.091%	.192%	7.0 to 7.5		144½	5′7½″
Sept. 13	350 to 375	90	70 to 80	404 to 429	57	1 plus	.212%	.214%	7.1 to 7.5		146½	5′7¾″

SEVENTH ANNUAL GRADUATE FORTNIGHT

OF THE NEW YORK ACADEMY OF MEDICINE

A Postgraduate Two Weeks Devoted to

DISEASES OF THE GASTROINTESTINAL TRACT

OCTOBER 22 TO NOVEMBER 2, 1934

The Program Comprises

AFTERNOON CLINICS, EVENING MEETINGS AND A SCIENTIFIC EXHIBIT

I. HOSPITAL CLINICS

Specially arranged clinical programs will be presented in sixteen of New York's leading hospitals. Among the clinicians who will participate are:

G. B. Bader	W. B. Farnum	J. M. Lynch	M. A. Rothschild
George Baehr	Hermann Fischer	A. B. MacLean	T. H. Russell
F. W. Baldwin	Ella Fishberg	Constantine MacGuire	F. B. St. John
F. W. Bancroft	L. F. Frissell	A. R. Mandel	L. F. Sanman
C. A. Barrett	Ross Golden	W. W. Maver	Bela Schick
F. H. Bartlett	A. W. Grace	F. L. Meleney	H. F. Shattuck
Fenwick Beekman	Carl Greene	H. W. Meyer	M. N. Shuster
G. E. Brinkley	R. H. Halsey	W. H. Meyer	DeWitt Stetten
A. S. Blumgarten	Joseph Harkavy	T. H. Morris	W. H. Stewart
Linn Boyd	I. W. Held	C. H. Nammack	Alfred Stillman
E. C. Brenner	Julius Hertz	G. T. Pack	Mills Sturtevant
T. W. Carey	J. W. Hinton	Douglass Palmer	R. P. Sullivan
H. W. Cave	C. P. Howley	H. S. Patterson	H. C. Thacher
J. E. Connery	W. M. Hunt	Marshall Pease	C. J. Tyson
A. C. Crump	H. E. Isaacs	Edward Peterson	Roy Upham
C. W. Cutler, Jr.	F. E. Johnson	Otto Pickhardt	P. P. Vinson
Roger Dennett	E. L. Kellogg	A. J. Quimby	W. L. Watson
E. J. Donovan	J. S. Leopold	H. A. Rafsky	A. O. Whipple
G. F. Dudley	Richard Lewisohn	E. J. Riley	W. C. White
Max Einhorn	Leopold Lichtwitz	Kingsley Roberts	I. O. Woodruff
A. A. Epstein	R. F. Loeb	Nathan Rosenthal	F. C. Yeomans

II. EVENING SESSIONS

The subjects and speakers at Academy meetings will be:

General principles involved in the diagnosis of gastrointestinal diseases	Harlow Brooks, Walton Martin, Robert E Pound
The applied physiology of the innervation of the gastrointestinal tract	A. C. Ivy
Constipation	Henry James Spencer
Diarrhea	John L. Kantor
Diseases of the esophagus	Carl Eggers
Functional and nervous diseases of the stomach	Burrill B. Crohn
Diseases of the pancreas, especially acute pancreatitis and its treatment	John Douglas
Disorders of the gastrointestinal tract in children	Rustin McIntosh, W. McKim Marriott, Charles E Farr
So-called chronic appendicitis	Charles F. Tenney
Acute appendicitis	John E Jennings
Peritonitis	Chas Gordon Heyd
Peptic ulcer	Arthur F. Chace, Eugene H. Pool
Carcinoma of the stomach	Fordyce B St. John
Jaundice	Reuben Ottenberg
Gallbladder and biliary passages	William W. Herrick, Allen O Whipple
Tumors of the colon	John F. Erdmann
Diseases of the anus and rectum, including tumors	Harvey B Stone
Colitis	Walter A. Bastedo, Thomas T. Mackie, Francis W. O'Connor
Intestinal obstruction	Arthur M. Wright
Diverticulitis	Dean Lewis

III. SCIENTIFIC EXHIBIT

An extensive scientific exhibit bearing upon the various aspects of the general subject will be held at the Academy concurrent with the Fortnight. Lecture demonstrations at regular intervals will be given by many of the exhibitors.

A COMPLETE PROGRAM AND REGISTRATION BLANK WILL BE MAILED ON REQUEST

PROCEEDINGS OF ACADEMY MEETINGS
MAY

STATED MEETINGS—May 3

I Executive Session—a Reading of the Minutes, b Election of Fellows and Members, c Presentation of diplomas

II The Hermann Michael Biggs Memorial Lecture—"*Causes and Prevention of Blindness*"—Arthur J Bedell, Albany

THE HARVEY SOCIETY (in affiliation with the new york academy of medicine)
May 17

The Eighth Harvey Lecture, "The Nervous Mechanism of Circulatory Control, Detlev W Bronk, Johnson Professor of Biophysics, University of Pennsylvania

SECTION MEETINGS

section of dermatology and syphilology—May 1

I Executive Session—Election of Section officers and member of Advisory Committee For Chairman, Ray H Rulison, For Secretary, E William Abramowitz For member of Advisory Committee, Fred Wise

II Presentation of Cases from Various Hospitals

III Discussion of Selected Cases

section of surgery—May 4

I Executive Session—a Reading of the Minutes, b Election of Section officers and member of Advisory Committee For Chairman, Guilford S Dudley, For Secretary, Condict W Cutler, Jr, For member of Advisory Committee, Ralph Colp

II Presentation of Cases—a 1 Complete removal of the lower eye lid for epithelioma One year result, 2 Sarcoma of the hand following irradiation for a benign lesion, Benjamin Rice Shore, b 1 Recurrent epithelioma of ala and floor of nose and of cheek following radium treatment Five year result, 2 Re implantation of ureter into renal pelvis for hydronephrosis, 3 Excision of massive congenital fibromatous pigmented mole of scalp, 4 Cannon shot wound of leg Pedicle flap graft from opposite thigh, Herbert Willy Meyer

III Papers of the Evening—a The management of the urological complications in injuries to the spine, John F Connors, b Cystic disease of the breast, Percy Klingenstein

IV General Discussion—Frank E Adair, Edwin Beer

joint meeting—section of neurology and psychiatry and the new york neurological society—May 8

I Executive Session—a Reading of the Minutes, b Election of Section officers and members of Advisory Committee For Chairman, C Burns Craig, For Secretary, Leon H Cornwall, For members of Advisory Committee, Irving Pardee, two years (to fill the unexpired term of Leon H Cornwall, resigned), Clarence P Oberndorf, five years

II Papers of the Evening—a Brain abscess, two recoveries in which the Mosher drain was used, Abraham Kaplan (by invitation), Discussion Joseph King, b Multiple sclerosis, brief presentations of patients on quinine therapy, Richard M Brickner, Discussion George H Hyslop, c Syndrome of tonic pupils and absent reflexes Walter Bromberg (by invitation), Discussion Harold Wolff (by invitation), d Disturbances in Gestalt function in psychoses and organic brain diseases, Lauretta Bender (by invitation), Discussion Max Wertheimer (by invitation), David M Levy

section of historical and cultural medicine—May 9

I Executive Session—a Reading of the Minutes, b Election of Officers and two members of Advisory Committee For Chairman, Russell L Cecil, For Secretary, Jerome P Webster, For members of Advisory Committee, Robert H Halsey, one year (to fill the unexpired term of Ira O Tracy, deceased), Eugene F DuBois, five years

II. Papers of the Evening—a. Historical points of interest on the mode of action and ill effects of mercury, E. William Abramowitz; b. Early 19th century dermatology and the Brothers Mahon, Theodore Rosenthal; c. Horace Wells and the discovery of anaesthetics, Walter R. Steiner, Hartford.

III. General Discussion.

SECTION OF PEDIATRICS—May 10

Case Demonstrations from 7:45 to 8:45—General Discussion 8:45

I. Executive Session—Election of Officers and member of Advisory Committee: For Chairman, Harry Bakwin; For Secretary, Alexander T. Martin; For member of Advisory Committee, Martha Wollstein.

II. Single Case Presentation will be given by the following hospitals: Mt. Sinai Hospital, Amyloidosis in a child of 8 years, Presented by J. Brem; Babies' Hospital, Sequestration of right upper lobe in the course of empyema, Presented by F. W. Solley; New York Hospital, A case of rat bite fever, Presented by W. S. Anderson; Polyclinic Hospital, General miliary tuberculosis in an infant of three months, Presented by W. Morgan Hartshorn; St. Vincent's Hospital, Schistosomiasis, Presented by Hugh Leahy; Lenox Hill Hospital, Pick's syndrome in a child of 12 years, Presented by J. L. Rothstein; St. Luke's Hospital, Amyotonia, Presented by Herbert F. Jackson; Hospital for Joint Diseases, Erythema nodosum—a link in a rheumatic syndrome, Presented by Irving Claman; Israel Zion Hospital, Thrombosis of the splenic vein, Presented by Harry M. Greenwald; Beth Israel Hospital, A case of rheumatic encephalitis (chorea insanias), Presented by Irving A. Frisch; Bellevue Hospital, Leukemia with extensive bone changes, simulating rheumatic fever, Presented by Lucy Porter Sutton.

JOINT MEETING—SECTION OF MEDICINE and SECTION OF ORTHOPEDIC SURGERY—May 15

(*Members of the Section of Orthopedic Surgery please note the change of date.*)

I. Executive Session—Reading of the minutes, Election of the Section Officers and members of the Advisory Committee. Section of Medicine: For Chairman, Randolph West; For Secretary, Paul Reznikoff; For member of Advisory Committee, Peter Irving. Section of Orthopedic Surgery: For Chairman, Leo Mayer; For Secretary, Walker Swift; For member of Advisory Committee, Paul C. Colonna.

II. Papers of the Evening—Symposium on Arthritis—a. From the medical standpoint; 1. Clinical aspects of acute arthritis, Walter L. Niles; 2. Laboratory aids in the differential diagnosis of acute arthritic conditions, Wendell J. Stainsby; 3. A medical viewpoint of acute arthritis, Ralph Boots; b. From the orthopedic standpoint; 1. The treatment of acute arthritis (surgical aspects), Allan DeF. Smith; 2. The operative treatment of chronic arthritis, Arthur Krida; 3. The non-operative treatment of chronic arthritis, Samuel Kleinberg.

III. General Discussion—Harlow Brooks, Percy W. Roberts, Philip D. Willow.

SECTION OF OTOLARYNGOLOGY—May 16

I. Reading of the Minutes.

II. Executive Session—Election of Section Officers and one member of Advisory Committee: For Chairman, Marvin F. Jones; For Secretary, Wallace Morrison; For member of Advisory Committee, Samuel J. Kopetzky.

III. Case Presentation—A pseudo-voice, probably esophageal, following total laryngectomy, Wallace Morrison; Discussion: S. Fineman, W. W. Carter, M. J. Myerson.

IV. Papers of the Evening—a. The treatment of old and recent fractures of the nose, Gerard H. Cox (by invitation); Discussion: Jay D. Whitham (by invitation), W. W. Carter; b. Report on the anatomical study of two hundred petrous portions of the temporal bone, Mervin C. Myerson, Herman Rubin (by invitation), Joseph G. Gilbert (by invitation); Discussion opened by: Ralph Almour; c. The historical development of the surgical treatment of post-otitic brain abscess, Leo M. Davidoff; Discussion opened by: Charles A. Elsberg, Joseph E. J. King; d. Adenoma of the bronchial mucous glands (lantern slides), B. M. Fried (by invitation).

V. General Discussion.

SECTION OF OPHTHALMOLOGY—May 21

I INSTRUCTION HOUR, 7 to 8 o clock—Demonstration of the stereoscopic treatment of heterophoria, David W Wells (by invitation)

II DEMONSTRATION HOUR 7 30 to 8 30 o clock—a Slit lamp studies, b Demonstration of anatomical specimens with slit lamp, Manuel U Troncoso (by invitation), c Case demonstrations

III SECTION MEETING 8 30 to 10 30 o clock—a Executive session, 1 Reading of the minutes, 2 Election of Section Officers and member of Advisory Committee For Chairman, Webb W Weeks, For Secretary, W Guernsey Frey, Jr, For member of Advisory Committee, Beroard Samuels, b Case reports, 1 A case of sympathetic ophthalmia, Frank C Keil, 2 Surgical approach of the levator through the skin, Daniel B Kirby, L Connor Moss (by invitation) Case 1 Ptosis, Case 2 Exophthalmos, 3 Melanoma of the conjunctiva—fatal termination, James W Smith, Scientific papers, 1 Meningiomas of the sphenoid ridge, Charles A Elsberg, Discussers John M Wheeler, Joseph E King, Thomas H Johnson, Cornelius Dyke (by invitation) 2 Cyclopia, Howard B Adelmann (by invitation), Discusser Charles R Stockard

SECTION OF OBSTETRICS AND GYNECOLOGY—May 22

I EXECUTIVE SESSION—a Reading of the minutes, b Election of Section Officers and member of Advisory Committee For Chairman, Harvey B Matthews, For Secretary, Walter B Mount, For member of Advisory Committee, David N Barrows

II PRESENTATION OF NEW INSTRUMENTS—A new catheter apparatus, Morris Leff, Discussion Harbeck Halsted

III PAPERS OF THE EVENING—a The production of active endometrium in the human castrate, Theodore Neustaedter, Discussion Robert T Frank, b The Robert s modification of the Pfannenstiel incision, Kingsley Roberts, Leon Loizeaux, Discussion A J Bullard, W T Kennedy, Harbeck Halsted, Max D Mayer, D W Tovey, c The barbiturates in primiparous labors, John T Tritsch (by invitation), Discussion, Harbeck Halsted, S J Scadron, Leon Loizeaux, G L Bowen, d The pelvic outlet—its importance in obstetrics, Joshua W Davies (by invitation), Discussion W T Kennedy

NEW YORK MEETING OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE UNDER THE AUSPICES OF THE NEW YORK ACADEMY OF MEDICINE—May 16

I Nervous control of thyroid activity, II Effect of thyreoactivator in absence of central nervous system, E Uhlenhuth

II Effect of Antuitrin S' vitamine on reproduction in rabbit, P D Rosahn, H S N Greene, C K Hu

III Observations on fowl paralysis (neurolymphomatosis), J Furth

IV Local cerebral anaphylaxis in the dog, L M Davidoff, N Kopeloff

V Hemorrhages in skin lesions after intravenous injection of starch, J Freund, W F Smith, Jr

VI Action of sodium salicylate on fermentation of salicin and glucose by streptococci, E Valentine, L Reiner

VII Antistreptolysin content of blood serum of children Its significance in rheumatic fever, M G Wilson, C W Wheeler, M M Leask (Introduced by O M Schloss)

VIII Electrocardiographic evidence of cardiac involvement in acute disease, A M Master, H Jaffe

AFFILIATED SOCIETIES

NEW YORK ROENTGEN SOCIETY (IN AFFILIATION WITH THE NEW YORK ACADEMY OF MEDICINE)—May 21

I 8 00 to 8 30 p m—Demonstration and discussion of interesting cases

II 8 30 p m—Some observations on the roentgen diagnosis of obscure lesions in the upper gastro intestinal tract, Geo W Holmes, Boston

III. General Discussion.

IV. Executive Session.

NEW YORK PATHOLOGICAL SOCIETY (in affiliation with the New York Academy of Medicine)—May 24

I. Demonstration of Pathological Specimens—a. Mitral stenosis with inter-auricular insufficiency, Seaton Sailer (by invitation).

II. Papers of the Evening—a. Synoviomata: report of three cases, Leila Charlton Knox; b. Hypertension and obesity associated with malignant adenoma of the adrenal and a pituitary chromophobic adenoma, Joseph J. Bunim (by invitation), Antonio Rottino (by invitation), Irving Graef; c. Some observations on the morphology of glandular hyperplasia of the prostate, Robert A. Moore.

III. Executive Session.

SECTION OF GENITO-URINARY SURGERY

The following were elected at the April meeting of the Section: Chairman, Augustus Harris, Secretary, Joseph A. Hyams; Member of Advisory Committee, George F. Hoch.

No May meeting of this Section was held.

RECENT ACCESSIONS TO THE LIBRARY

American society of clinical pathologists. The medicolegal necropsy.
Balt., Williams, 1934, 167 p.

Bache, L. F. Health education in an American city.
Garden City, Doubleday, 1934, 116 p.

Ballance, (Sir) C. A. The Lister memorial lecture . . . 1933.
Dundee, Thomson, [1933], 77 p.

Billroth, C. A. T. Historical studies on the nature and treatment of gunshot wounds. . .
New Haven, Nathan Smith Med. Club, 1933, 82 p.

Chauvois, L. Circulation du sang (schéma nouveau).
Paris, Baillière, 1933, 172 p.

Clinique (La) urologique de Necker, 1912-1933.
Paris, Masson, 1933, 305 p.

Emerson, H. Alcohol, its effects on man.
N. Y., Appleton-Century, 1934, 113 p.

Fujikawa, Y. Japanese medicine.
N. Y., Hoeber, 1934, 114 p.

Gutman, J. Modern drug encyclopedia and therapeutic guide.
N. Y., Hoeber, 1934, 1393 p.

Haggard, H. W. Mystery, magic, and medicine.
Garden City, Doubleday, 1933, 192 p.

Harrow, B. & Sherwin, C. P. The chemistry of the hormones.
Balt., Williams, 1934, 227 p.

Heidel, W. A. The heroic age of science.
Balt., Williams, 1933, 203 p.

Heitzmann, L. Urinary analysis and diagnosis. 6. ed.
Balt., Wood, 1934, 385 p.
Iyer, T. G. R. The hand book of Indian medicine.
Fort, Erode, Sri Vani Vilas Press, 1933, 540 p.
Jeanselme, E. Le lèpre.
Paris, Doin, 1934, 679 p.
Jennings, H. S. The universe and life.
New Haven, Yale Univ. Press, [1934], 94 p.
Kerney, E. A glossary of French medical terms referable to the eye.
N. Y., Institute of French Studies, 1934, 209 p.
Killian, H. Facies dolorosa.
Leipzig, Thieme, 1934, 88 p.
McIver, M. A. Acute intestinal obstruction.
N. Y., Hoeber, 1934, 430 p.
Merry, R. V. Problems in the education of visually handicapped children.
Cambridge, Harvard Univ. Press, 1933, 243 p.
Naegeli, O. Allgemeine Konstitutionslehre. 2. Aufl.
Berlin, Springer, 1934, 190 p.
Olivecrona, A. H. Die parasagittalen Meningeome.
Leipzig, Thieme, 1934, 143 p.
Ormsby, O. S. A practical treatise on diseases of the skin. 4. ed.
Phil., Lea, 1934, 1288 p.
Parsons, T. R. Fundamentals of biochemistry. 4. ed.
Cambridge, Eng., Heffer, 1933, 435 p.
Penrose, L. S. The influence of heredity on disease.
London, Lewis, 1934, 80 p.
Principles and practice of physical therapy, edited by H. E. Mock, R. Pemberton, J. S. Coulter.
Hagerstown, Prior, 1934, 3 v.
Rathbone, J. L. Corrective physical education.
Phil., Saunders, 1934, 292 p.
Reid, W. D. Teaching methods in medicine.
[Boston, author, 1933], 111 p.
Roffo, A. H. & Thomas, J. La chimie du cancer.
Paris, Vigot, 1933, 339 p.
Salmon, M. & Dor, J. Les artères des muscles des membres et du tronc.
Paris, Masson, 1933, 238 p.
Schwesinger, G. C. Heredity and environment.
N. Y., Macmillan, 1933, 484 p.
Sure, B. The vitamins in health and disease.
Balt., Williams, 1933, 206 p.
Vehrs, G. R. Spinal anesthesia; technic and clinical application.
St. Louis, Mosby, 1934, 269 p.
Westhues, H. Die pathologisch-anatomischen Grundlagen der Chirurgie des Rektumkarzinoms.
Leipzig, Thieme, 1934, 113 p.

DOCTOR WILLIAM HENRY WELCH
1850-1934

An Honorary Fellow of The New York Academy of Medicine

Doctor William H. Welch was born in Norfolk, Connecticut, on April 8, 1850, and died in the Johns Hopkins Hospital, Baltimore, on April 30, 1934. He was the outstanding figure in American medicine, and his international reputation was such as to place him in the forefront among his medical contemporaries. The range of Doctor Welch's intellectual powers was so large, and the fascination of his presence so captivating, that he may be said to have become the most revered and beloved physician of his time. No utterance of his, whether in the realm of science, literature, the arts, or history failed to arrest attention by reason of the learning and charm revealed. The encyclopedic nature of Doctor Welch's mind made it possible for him successively to fill the chairs of pathology, hygiene, and the history of medicine at Johns Hopkins University. He resigned the professorship of pathology at the age of sixty-five, only to take up the professorship of hygiene, which in turn he relinquished at seventy-five, to assume the professorship of the history of medicine. And in all these undertakings he was a pioneer, creating the opportunities and producing the means by which they could be realized. Doctor Welch may be said to have brought the modern pathology to the United States, and to have organized his laboratory with a comprehensiveness which placed it at once in advance of the best European models. Before Doctor Welch's day there was no school of hygiene in this country, and none in a fully developed state anywhere; the school which he designed and put into operation quickly became the model of the world. And before the Institute of the

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A biographical sketch of Dr. Welch, by the author, is included in "Papers and Addresses," published on his 70th birthday, in 1920. It may be consulted for a fuller and more systematic account of the main incidents of Dr. Welch's professional life. The sketch was reprinted in *Science*, 1920, 52, 417. Brief summaries are also available in "American Men of Science," 5th edition, 1933; and in "Who's Who."

History of Medicine was created by him, no such school existed outside of Germany.

Doctor Welch came from a family of physicians. His father and four of his father's brothers, his grandfather and great-grandfather were physicians. Doctor Welch entered Yale College in 1866 and was graduated in 1870, third in his class. He taught school one year, and then entered the College of Physicians and Surgeons in New York City, but only to leave and return at once to New Haven for a year of extra study in chemistry at the Sheffield Scientific School and the Yale Medical School. This early deviation from the ordinary course of events in the study of medicine must have seemed arbitrary, and yet it cannot be so regarded now. There was a kind of prescience in the act, since it showed that he appreciated well in advance of prevailing beliefs the important role which chemistry would come to play in the science and art of medicine. Doctor Welch returned to the study of medicine in 1872; and the even tenor of his progress through college was perturbed by what ordinarily would be an inconspicuous event. He won as a prize in the course in neurology a microscope fitted with superior lenses. This success had two consequences, one important, the other of passing interest. The microscope "produced the spark which ignited the tinder of a latent interest in pathology," and it led to a desire to specialize in diseases of the nervous system, which latter did not survive the German experience still a few years distant.

Following graduation, there was a not unusual period of struggle in New York, lasting two years; and then in 1876, together with his friend and fellow townsman, Doctor Frederick S. Dennis, we find Doctor Welch embarking for Europe. This is not the place in which to describe the fruitful two years of European study which followed, but it is necessary to record another significant departure from the usual course pursued by medical students. Doctor Welch offered himself to, and was accepted by the leading physiologist, Carl Ludwig, professor at the University in Leipzig. That Doctor Welch had perceived the importance of phys-

iology for the impending growth of scientific medicine is another example of the penetrating power of his intelligence. Moreover, this choice was to lead to a still greater piece of good fortune, for it directed Doctor Welch's specifically pathological studies into an unusual channel, and away from Virchow and his school, the center of interest at the time, to Cohnheim and physiological pathology, which was to provide a firmer and more immediate foundation for experimental medicine. Associated with Cohnheim were the brilliant, young investigators, Weigert and Ehrlich, soon to open new vistas in pathology. They and Doctor Welch proved congenial; and intimate, enduring friendships followed. There is always the temptation to attribute to accident these fortunate happenings in the careers of eminent men. Given Doctor Welch's endowments and the circumstance that he came under Cohnheim's influence—the result of his studies with Ludwig—the rest succeeded unavoidably, namely the rewarding relations with Weigert and Ehrlich, the early contact with Robert Koch, and most important of all, the call to the Johns Hopkins Hospital at Cohnheim's suggestion.

To pursue extra studies in chemistry as a preparation for medicine, to seek a physiological foundation for pathology, simply meant, as soon became apparent, that Doctor Welch's compulsion was to delve deeply into the springs of knowledge. This compulsion reveals itself in all phases of his subsequent career, whether he is carried into the new fields of hygiene and preventive medicine, into historical studies, or into the cultivation of literature or the arts, the beginnings of which are lost in the remote days of his early youth. A mind thus constituted does not stop abruptly at a given boundary. Those intimates of Doctor Welch who were privileged to pass beyond the barrier of his unusually modest reticence, soon discovered that his knowledge of belles-lettres, poetry, music and the other arts, rivalled that of medical science and lore. There resulted from this happy concatenation of forces a remarkably rounded and complete personality, in which no one highly specialized interest absorbed all the available powers to the

exclusion of other and diverse, momentous interests to which the human spirit might respond.

Doctor Welch returned to New York in 1878, the future uncertain, and the next half dozen years were spent in a medley of activities: Goldthwaite's quiz, pathology at Bellevue Hospital and Bellevue Medical College, practice, association with the elder Flint then engaged on his "Practice of Medicine" to which Doctor Welch contributed the chapters on general and special pathology, constituting virtually a treatise on the subject which even today possesses intrinsic as well as historical interest.

The appointment to the professorship of pathology at the Johns Hopkins University was made in 1884. Thus it came about that in April, 1934, Doctor Welch's eighty-fourth birthday and the fiftieth anniversary of his residence in Baltimore could be celebrated jointly. Messages of affection and admiration came from near and far; and Doctor Welch was hailed not only as leader in medicine, but as first citizen of Maryland.

In 1884, the Johns Hopkins Hospital was still incomplete and the Johns Hopkins Medical School still merely an aspiration which was to be realized ten years later. The new bacteriology had just been brought into being by Koch and his early, gifted pupils; hence Doctor Welch returned to Germany to acquire the technique of this new branch of learning destined soon to open a new and brilliant era in medical progress. There repaired to Germany also at this time, Doctor T. Mitchell Prudden, whose career in pathology in New York was second only in importance to that of Doctor Welch in Baltimore. These fellow students at Yale, fellow pathologists in New York, were to meet again in Koch's laboratory in Berlin, and to renew and strengthen ties of mutual purpose and friendship which were to unite them in many subsequent undertakings of a philanthropic and professional nature.

Although Doctor Welch remained all his life a cosmopolitan in education, yet it was the long Baltimore period of his activities which established his fame and made him

the statesman and prophet of modern medicine in the United States. He brought together the first faculty of the Johns Hopkins Hospital and Johns Hopkins Medical School, he guided the events which placed the Johns Hopkins Medical School at its inception on a high level of teaching, scholarship, and research; hence he, more than anyone else, was responsible for the amazing advances made in medical education in the United States during the past forty years.

During the pregnant half century of Doctor Welch's Baltimore professorates, his extraordinary energies had scarcely abated until the onset of his last illness. Thus he continued active mentally and physically almost until the end; and throughout these five decades he was distinguished as the brilliant teacher, successful investigator, broad scholar, charming companion, and wise counselor. No one was called on more than he to advise in important educational and philanthropic enterprises; to these appeals Doctor Welch gave his time without stint. Doctor Welch's printed papers and addresses collected and published on his seventieth birthday make three noble volumes. They are a treasure house of knowledge and wisdom, and they cover an altogether extraordinarily broad expanse of learning.

And no one was endowed with a warmer heart than Doctor Welch, who appeared gifted with the secret of perpetual youth, for his wide interests never waned, and he formed deep and affectionate friendships with succeeding groups of younger men. In short, Doctor Welch may be said to have warmed both hands at the genial flame of life, and to have been inspiration, guide, joy, and delight to many men.

SIMON FLEXNER.

DEATH OF FELLOW

DOTY, ALVAH HUNT, M.D., 110 Monterey Avenue, Pelham, N. Y.; graduated in medicine from Bellevue Hospital Medical College in 1878; elected a Fellow of the Academy March 5, 1891; died May 27, 1934. Dr. Doty was a member of the State and County Medical Societies, the American Medical Association, and the American Public Health Association. Dr. Doty was health officer of the Port of New York from 1895 to 1912.

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CLINICAL AND BIOLOGIC CONSIDERATIONS OF OBESITY AND CERTAIN ALLIED CONDITIONS*

ALBERT A. EPSTEIN

Obesity is a commonplace condition. Fashion makes it a frequent topic of conversation, and the attention of the physician is directed to it more often by a patient's desire to reduce for aesthetic reasons, rather than for reasons of health. Our interest in the subject, however, should be based upon the fact that certain dangers are inherent in obesity. The susceptibility of obese individuals to infectious diseases, to diabetes, and to the degenerative diseases of the cardio-vascular system, as well as the higher mortality from all causes in the obese as compared to the non-obese, are well known facts, and are all questions which render the subject worthy of the most serious consideration. The approach to the subject, however, is extremely difficult because the literature, both professional and lay, is as you know replete with information both relevant and irrelevant.

*Delivered October 31, 1933.

Our scientific knowledge of obesity may be said to be in a state of flux, and by no means final. Obesity constitutes a problem in which nearly all phases of metabolism are represented, and in which the specific physiology of every organ and tissue in the body is somehow concerned.

Properly defined, obesity signifies an increase in body weight in excess of the limitations of skeletal and physiologic requirement, due to the deposition of fat. Common usage has made the term synonymous with adiposity, lipomatosis, and in fact all forms of corpulency irrespective of their nature or origin. This broad use of the term obesity is not accidental; it is the result of the difficulties which attend all attempts at sharp clinical differentiation.

It is customary to divide all cases of obesity into two general groups: the exogenous and the endogenous. The term exogenous is applied to those cases in which the obesity is due either to overeating or lack of exercise; a purely mechanistic conception in which the principle of the conservation of energy is believed to be operative. The term endogenous is applied to cases in which the obesity cannot be ascribed to overfeeding or underexercise alone, but in which an additional factor is concerned. Cases in this group often present evidence of glandular dysfunction, hence the term endocrine obesity has been introduced. Endocrine is however, a specific term and should be applied only to those cases in which a definite glandular etiology can be established. The designation of obesity as exogenous or endogenous is often merely a matter of point of view, based upon the therapeutic experience of the observer.

An increasing number of investigators are of the opinion that, with but a few exceptions, obesity is the result of alimentary maladjustment in which food intake exceeds energy output, and that this process may be reversed by proper dietary restrictions. There are still others, however, who hold to the view that tissue preparedness, conditioned by constitutional and hereditary factors, is essential for the deposition of fat.

While fat may be the chief substance deposited in the tissues, most observers agree that not all cases of corpulency are necessarily of that origin. Other substances such as mucin may be deposited, or even the overdevelopment of structures other than the adipose tissue may contribute to the final result.

For a proper understanding of the subject, the following questions must be considered: 1. What is the normal weight of an individual and how is it maintained at a constant level? 2. If stability in weight is the resultant of a mechanism which functions constantly and which adjusts food intake to energy output, then what is it that initiates a departure from the normal which permits an increment in weight? 3. Does tissue activity alone control and regulate the demand for food, and are hunger and appetite the result of that demand? 4. How are the various nutrients constantly present in the body utilized, and what relation do they bear to oxidative processes and tissue activity? 5. What role do the endocrine glands play in the regulation of metabolic processes and tissue activity, and how does disease or dysfunction of one or another of these glands affect this regulation?

The first question to be considered is the normal weight of an individual which is commensurate with his skeletal and physiologic requirements. For this there is no absolute standard. Certain values have been arrived at from a comparison of the weights of large numbers of presumably normal persons and the law of averages applied. Such a method permits a variation of at least 10 per cent in either direction. Hence, while the weights given in standard tables are very useful, discretion must be used in their clinical application. Experience teaches that small excesses in weight, or the reverse, may be disregarded in the otherwise healthy individual.

What is the mechanism then which maintains the weight of an individual at normal? This is the key to the solution of the whole problem of obesity. Food is the source from which the energy developed by the body is derived. Since

the law of the conservation of energy still holds good, it is necessary to conclude that the maintenance of a constant weight represents the resultant of an adjustment between the potential energy supplied by food and the active or kinetic energy expended by the body. Normally there is an automatic regulation of the output of energy and the intake of food. An adult after having attained an optimum weight, that is a medium average of nutrition, adjusts himself to a definite amount of food that constitutes for him the so-called maintenance diet which deviates upward and downward from the average according to the varying demands created by a varying amount of physical labor performed. Of course, the exact amount of food that corresponds to the consumption of energy for each day is not introduced during each 24 hour period. These differences become so completely equalized by small increases and decreases, that many persons maintain their weight at a fixed level for a period of years. This finely adjusted normal regulatory mechanism is occasionally disturbed, sometimes forcibly, but more frequently by the accumulation of slight influences producing a large effect, as for example, when the expenditure of energy remains constant, and the food intake is increased but slightly. Small excesses of food over the usual amount are sufficient to upset this balance. Assuming that the daily surplus amounts, on an average, to 200 calories, which is contained in 1½ glasses of milk, an ounce of butter, ¼ pound of meat, or 2 ounces of bread, let us note the result.

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are conspicuous for their tendency to cause weight increase; they are not used in place of other articles of food, but are generally added to a diet that is in itself already sufficient to maintain nutrition. Under these circumstances the complete caloric value of the alcohol becomes utilized as a means of fattening. This is readily appreciated when it is realized that one ounce of alcohol protects approximately its equivalent in weight of fat from combustion which may remain stored in the body.

As a corollary to the preceding, increase in weight may result when food intake remains the same but energy consumption is decreased. The desire for food and the actual intake of food under normal conditions, correspond to the increase or decrease of energy output. Occasionally this regulatory adjustment is interrupted, particularly when individuals who have been accustomed to strenuous labor, or much exercise, suddenly change their occupation or habits, and begin to lead a less active life. In men this frequently occurs towards the fifth decade of life, or somewhat later, in women about ten years earlier. While the habits in regard to the amount of food consumed may remain the same as in previous years, less energy is expended, so that what was formerly an adequate diet, now becomes a surplus one. These factors may produce either slowly or rapidly an increase in the fat deposits of the body. Of course external circumstances, of the character described above, are not the only causes that may lead to a more sedentary method of life, disease for instance, may cause such a change in habits, especially disturbances of circulation, diseases of the respiratory apparatus, of the nervous system or the organs of locomotion. While physical activity is a potential element in the constancy of weight, it must not be assumed that it is the only source of energy responsible for this balance. Energy output represents the summation of three metabolic processes, a disturbance in any one of which may contribute to an imbalance between the intake and output of energy. They are: 1. the basal metabolic rate, representing the sum of

all the oxidative processes of the body when completely at rest; 2. the accessory oxidative processes due to the specific dynamic action of food; and 3. the accelerated metabolism or oxidative processes due to work or exercise.

The applicability of the principle of the conservation of energy to the maintenance of weight equilibrium cannot be denied, but its operation is not always apparent, nor can the automaticity of the operation be so easily explained. For there are many persons who eat much without ever showing any increment in weight, while others gain weight with remarkable facility. Moreover another circumstance which is not entirely in accord with the view that weight equilibrium is the simple result of a balance between food intake and the amount of energy liberated, is the fact that reduction in food intake below energy output does not always yield uniform results. It is this incompatibility in the mechanistic concept of obesity which presents the greatest difficulty. This view has caused much speculation and has given rise to a number of different theories. It would take us too far afield to discuss them at length; yet they cannot be dismissed without some consideration.

The dependence of food intake on appetite and its relation to tissue activity is a very complex problem; for example, demand for food can increase without increase in tissue activity and is well illustrated in lesions of the brain, particularly those in the hypothalamic region. Deprivation of an essential nutrient, as in diabetes mellitus, may cause an increase in demand for food without augmentation of tissue activity. Increase in tissue activity may occur without increased demand for food, as in hyperthyroidism, fevers, and cachectic states.

Certain investigators claim to have demonstrated the occurrence of a "negative phase" or temporary depression in metabolism after light exercise and following the ingestion of food. They regard this as important in the maintenance of weight equilibrium. A confirmation of these findings would be extremely helpful in understanding this problem.

Recently the view has been advanced that weight stability is of very much the same nature as temperature stability, and that the determining factor resides within the brain. This view is based upon experimental and clinical evidence in which it was noted that injury or disease of the hypothalamic region, as already alluded to, is followed, often very promptly by excessive increase in weight. Stability in weight is not necessarily characteristic of the individual of normal weight; such stability is often present for long periods of time both in the obese as well as in the undernourished individual.

None of the foregoing hypotheses adequately explains the mechanism which maintains the weight of an individual in equilibrium. This being the case, it is self evident that any attempt to elucidate the origin of obesity is even more difficult.

Obesity is so obviously a departure from the normal state that it is natural to seek its explanation in deviations of metabolism from the normal. Thus, reduced activity of the tissues, as evidenced by lowered metabolic rate; reduced kinetic response of the tissues to food, i.e. refractoriness to the specific dynamic action of food; increased formation of fats from carbohydrates; improper oxidation of fats, etc. have been regarded as primary or contributory causes of obesity. But a careful analysis of the available information on these questions fails to reveal any dependable evidence indicating that any or all of the metabolic processes just mentioned are definitely responsible for the development of obesity. This may be in part due to the fact that the bulk of our information is derived from observations on individuals already obese; the metabolic observations noted are irregular, inconstant, or often too trifling to be conclusive. A characteristic of the living organism is its adaptability to changed conditions. Obesity is a condition which is usually slow in development, so that the absence of any evidence of a metabolic disturbance in an obese individual is no indication that such a disturbance does not exist at the outset. The final state of the meta-

bolic processes as ascertained may represent the end result of a long series of adjustments by means of which a balance has been established.

Newburgh has shown that in obese patients the energy expenditure is less than the caloric intake, and that a positive energy balance exists. He has also shown quite definitely that if the energy intake be reduced below the output, these patients will lose weight. This is in conformity with the original definition of obesity, but does not explain why obese patients consume more food than they require to maintain their established weight, or why their energy expenditure on a given caloric intake is less than that of normal people. This is a strictly mechanistic viewpoint which explains the ultimate effects of overfeeding and accounts for the so-called exogenous obesity, but gives no hint as to the initial cause of the increased consumption of food and its consequences.

An answer to this query is to be found in the conclusions recently arrived at by Strang and Evans, who maintain that the active tissues of the body are chiefly concerned in the elaboration of the metabolic processes and that adipose tissue itself is relatively inactive. Hence, they conclude that all computations should be based upon the mass of active tissue in the body. If this manner of computation is employed, it is found that the metabolism of active tissue must be considerably above normal in order to maintain metabolism at the estimated level; whereas the metabolic rate based upon surface area may be normal, or less often subnormal in the obese. From their results, it would appear that tissue activity in obesity is not reduced but actually increased.

The question arising at this point is: What is the mechanism which permits obese persons to remain for a long time on a positive energy balance; why do they continuously exceed their caloric necessity? Attention should be directed to deviations in the normal relationship between appetite on the one hand, and energy expenditure on

the other. When this relationship is in perfect adjustment, as it is normally, no obesity develops; but, when appetite exceeds energy requirement obesity appears.

There is no evidence to prove that increased appetite is the primary cause of obesity. It is conceivable that another factor, "The undeterminable tendency to obesity", may in itself be responsible for the increased appetite. Putnam, Benedict and Teel have shown experimentally that there is a relationship between growth and appetite, and if we compare obesity to growth in general, it is fair to admit that appetite is the result and not the cause of the process.

The concept of the endogenous nature of obesity does not deny the principle of the conservation of energy, it goes a step further and attempts to explain the mechanism on the basis of an hereditary or constitutional predisposition. The terms "hereditary and constitutional" as related to obesity do not lend themselves to specific definition, and may in the last analysis signify a cryptic disorder of the endocrine glands. Increased tissue avidity or lipophilia appears as a corollary to the constitutional concept of obesity. The effects of central disturbances on body weight, as well as the selective and characteristic distribution of fat in thyroidal, gonadal and pituitary dysfunctions lend support to this view. Moreover, under certain conditions, the general body fat may disappear without affecting the localized deposits.

Contrary to the view presented earlier in this discussion, some investigators are of the opinion that the position of adipose tissue in the animal economy is not that of a passive structure, but is the seat often of very active changes, affecting specifically the relations between carbohydrate and fat metabolism. It is believed that fat cells are capable of converting carbohydrates into fat. The presence of glycogen in these cells, under certain conditions, is interpreted as indicating such a process. It has also been suggested that nerve as well as hormonal influences play a part in this process.

To summarize, the deposition of fat in varying degree is present in all types of obesity, the only distinction being the rate of deposition or its distribution. In exogenous or generalized obesity an increase of adipose tissue usually occurs in the normal depots.

Considered practically, therefore, the first problem which concerns the physician is that dealing with the accumulation of fat.

In the early stages of life, a certain degree of obesity is regarded as physiologic and the excess weight represents a reserve of material and a potential source of energy, while the obesity of the latter period of life is regarded as unphysiologic, because of the many true and alleged ill effects which it may produce. Normally, adipose tissue is an important element in the structure of the body and constitutes approximately 22 per cent of its weight. Thus obesity may represent, on the one hand, a temporary normal expedient and on the other a process or condition which is probably physiologic in its origin and pathologic in its consequences.

Fortunately, unless and until the obesity causes definite pathologic changes, the conditions leading up to it are reversible, and with a reduction in food intake over the energy output, fat is ultimately mobilized from its depots and utilized as body fuel. This forms the principle upon which the modern treatment of obesity is largely based. Recent investigations support more and more the mechanistic concept of obesity and all therapeutic procedures employed rely upon this concept.

The distribution of body fat may be very widespread and some vital organs may become affected. In universal or general obesity, the magnitude and distribution of fat is not uniform throughout the body. Some localities acquire increments earlier than others and possess the capacity of storing fat to a greater degree. Fat, sometimes in enormous quantities, is lodged in the subcutaneous and intramuscular tissues, the bone marrow, the mesentery, the omentum, and retroperitoneal tissue, the epicardium, the

tissues about the kidneys, and the orbit. In extremely obese persons the fat after filling these places to their utmost, seems to overflow into unexpected localities, such as the wall of the heart and also beneath the endocardium; it pushes apart the lobules of the pancreas and spreads around to the free surface of the intestines. This distribution is characteristic of all cases of alimentary obesity, but it does not apply to those obesities in which hormonal or endocrine influences play a part. In these cases the normal depots may remain unaffected, while unusual locations are chosen for the deposition of fat.

As previously pointed out, the excess weight in the obese person is not always due to fat alone. Thus the outward manifestations and consistency of the panniculus show striking variations, such as texture, mobility and attachment of the skin to the underlying tissues. This can be readily appreciated when the character of the obesity usually encountered in men is contrasted with that of women, except in those women under forty in whom the obesity is due to deliberate overeating.

In the matter of the obesities now to be considered, which are due to failure on the part of one or another endocrine gland, there are certain general principles to be borne in mind. The first is that many an obesity of primary alimentary origin becomes complicated by elements of endocrine failure. In very pronounced cases of general obesity, evidences of thyroid inadequacy are often present. When particularly outspoken, the case is liable to be regarded and treated as one of hypothyroidism or myxedema, not only with indifferent success, but occasionally with the provocation of untoward symptoms. It is also necessary to remember that an endocrine obesity nearly always denotes failure, relative at least, of more than one gland, and that it is in fact very often a pluriglandular rather than a monoglandular syndrome.

The thyroid type of obesity is too well known to require any detailed description. Its development is proportionate to the degree of thyroid deficiency. It constitutes in

reality a pseudo-obesity; the deposition of fat is incidental and the corpulency is due to the deposition of mucinous or myxedematous tissue, with a special predilection for certain localities.

Dysfunction or cessation of the endocrine activity of the procreative glands is accompanied by the development of obesity, both in the female and the male. The climacterium in the female, whether artificial or spontaneous, is followed as a rule by a corpulency which is not distinguishable from that which accompanies hypothyroid states, and may in many instances be accompanied by an actual hypofunction of that gland. The metabolic accompaniments of a true hypothyroidism are not frequently demonstrable in this type of obesity.

The type of obesity due to interference with the testicular hormone varies with the cause. It is necessary to distinguish between the results of a surgical castration, and the effects of lack of development or atrophy of the testicles. Differences in the clinical manifestations depend upon the stage in sex development in which castration occurs, that is, before or after puberty.

I shall not enter into a detailed description of these various conditions, as they are amply described in most textbooks. Suffice it to say that in pathologic hypogonadism the close approach of the individual to the feminine type serves to implicate these glands.

The chief difficulty in the differential diagnosis of endocrine obesities lies between the type due to gonadal insufficiency and that which results from deficiency of one or both lobes of the pituitary. Perhaps the most important differential point is that in strictly gonadal insufficiency, obesity is a late manifestation, whereas in the pituitary inadequacy it is more likely to appear early. Differences in skeletal development may be of assistance in establishing the true origin of the associated obesity. Generally speaking obesity of pituitary origin is a girdle obesity; the adipose tissue is deposited chiefly in the area which is

bounded above by the diaphragm and below by the knee. When there is a conspicuous deposit of fat in any area outside this region, it is almost always due either to alimentary causes or to a concomitant defect in some other gland; the glands most commonly involved being the gonads.

Unlike the exogenous type of obesity, that due to endocrine disturbance is sometimes accompanied by changes in the metabolic reactions. Those due to hypothyroidism, particularly those of severe degree, may show definite reduction in the basal metabolic rate, and a disposition to increases in the lipoid content of the blood, a diagnostic point of considerable importance. Increase in carbohydrate tolerance may also be observed. Those of pituitary origin show little or no change in the metabolic rate, slight if any increase in lipoid content of the blood, but occasionally a decided decrease in carbohydrate tolerance; while those of gonadal origin may show no other abnormalities than a moderate or considerable increase in the lipoid content of the blood. Again attention must be called to the fact that, in most instances, the endocrine type of obesity is rarely due to a decrease or cessation of function in one gland alone, so that the distinguishable features in respect to the metabolic aberrations just mentioned, are not always clearly defined or constant.

In all the aforesaid, emphasis has been laid particularly upon the causes of overweight; first and most important is fat; then the non-adipose tissue such as mucinous substance and the like. There is, however, one other substance which contributes to obesity in a large measure, namely water. The association of water retention with obesity is so constant that its occurrence cannot be regarded as casual or accidental. I am inclined to the view that the retention of water is a necessary concomitant of fat deposition. The relation which they bear to one another is regulated by the biophysical and biochemical state of the colloids of the blood and the tissues; an excellent example of this regulation is to be found in nephrosis. To put it in a word, obesity represents a lipedema, a migration and

deposition of water and fat to the various tissues of the body, and can arise from causes originating from within, or may be induced by extraneous factors. This concept aids in elucidating a number of questions. Time will not permit me to discuss the evidence. Suffice it to say that in devising therapeutic procedures and in analyzing their effects, water metabolism must be taken into strict account.

Mineral salts are closely associated with water retention. Gamble, Ross and Tisdale have demonstrated certain facts regarding water and mineral metabolism, indicating that the sum and total of chemical bases is important in maintaining the structural integrity of the body fluid. They computed the weight of water lost during fasting in terms of fixed bases, and have demonstrated that losses up to 62 per cent of body weight may be due to water. There are many cases of obesity in which retention of water and salt may be wholly unsuspected. These patients when dieted strictly may be greatly undernourished yet suffer no apparent loss of weight because of water storage. Von Noorden in 1910 already warned about the importance of water and salt retention in the treatment of obesity. Zondek designated such patients as the "salt-water-obesity type"; Bauer speaks of them as cases of "hydrolipomatosis". The water balance in obese persons has been accurately studied by Newburgh and his associates; they have shown that obese individuals kept on a strict metabolic regime may hold, or even gain weight due to water retention. Certain complicating factors common to obesity must be reckoned with when interpreting the relation of overweight to retention of fluid; chief amongst these is circulatory inadequacy and cardio-vascular disease.

It is quite obvious that whatever the ultimate mechanism underlying fat deposition or water retention may be, in applying therapeutic procedures to obesity, these facts must be [illegible] in mind and seriously considered. Frequently suc[illegible]re depends upon the proper interpretati[illegible]ons.

In discussing the complications of obesity, we must distinguish two sets of conditions, namely, those in which complications occur in an already established obesity, and those in which obesity is a sequel to other diseases. In the first category belong cardio-vascular disturbances, diabetes, biliary diseases, gout and infections; in the second, orthopedic conditions, pulmonary tuberculosis, and primary cardiac disease; in other words, conditions in which sedentarism plays an important part.

It is common knowledge that obesity carries with it certain potential dangers which sooner or later manifest themselves clinically. Firstly, excess of adipose tissue frequently constitutes a mental and physical handicap, and tends to promote the very conditions which cause obesity and make it progressive. Secondly, and probably the most important, is the problem of cardio-vascular disturbances. As a result of the deposition of fat in the tissues, some of the smaller blood vessels must sooner or later yield to the greater pressure of the fat and compensatory circulation must be established. Failing this, the increased peripheral resistance may lead to an increased blood pressure. Because of this, increases in blood pressure, particularly in the earlier stages of obesity are not uncommon. On the other hand, in many cases of obesity of long standing, a low or subnormal pressure is encountered, unless still other conditions complicate the picture. The cause of the fall in blood pressure may in part be due to the establishment of compensatory circulation, which relieves the load in the peripheral circulation; or the pressure may fall because of cardiac insufficiency. Peable states that the mortality from heart disease in the obese is two and one-half times as great as in persons of normal weight. This effect upon the heart is in all probability the result of a number of causes which are operative in obesity, namely: 1. increase in peripheral resistance as mentioned above; 2. infiltration of the heart muscle itself, lessening its contractile power; 3. as Strang and Evans have shown, that while the basal meta-

bolic rate of the obese as measured in terms of surface area, is usually normal, the oxidative processes in the active tissues of the body are markedly increased; a circumstance in which the heart is greatly concerned. This fact gains particular significance from the recent work of Blumgart, who found that reduction in the oxidative processes of the body, i.e. diminishing the basal metabolic rate by ablation of the thyroid, serves to reduce the cardiac load and spares the heart when it is greatly embarrassed and decompensated; 4. water retention, which is so constant a phenomenon in obesity, may be a cause as well as a sequence of cardiac insufficiency. Clinical observations indicate that the simple removal of water from the body exerts a beneficial effect upon the heart and circulatory system in cardiac failure, and from this we may infer that water retention occurring in obesity plays an important part in embarrassing the heart and circulatory system. It is probably safe to say that many of the beneficial effects of reducing procedures, so far as the heart and the circulatory system are concerned, are in a large measure to be ascribed to the incidental removal of much stored water.

Another very important complication of obesity is diabetes. Many clinicians are of the opinion that obesity bears a direct etiologic relation to diabetes. This connection is so firmly established that to contradict it would seem like heresy, and yet I feel that the data can bear closer scrutiny. The association of obesity with diabetes is indeed common. Both diabetes and obesity frequently bear the character of familial diseases or conditions, the importance of which cannot be ignored in statistical deductions. When a familial or hereditary factor relative to diabetes exists in any individual, the advent or coexistence of obesity may conceivably hasten or induce diabetes; but, whether a diabetes would develop as a direct sequel of obesity, in a person free from hereditary taints, is very problematic. Obesity may bear a pathogenic relationship to diabetes, but whether it is the direct cause of it is still an open question.

Overfeeding is in most instances the direct cause of obesity. Overfeeding may play a part in the exhaustion of the vital organs, amongst others, the pancreas and the liver, and may lead to the development of diabetes. But whether or not an obesity once established is capable of producing these functional effects upon the vital organs is by no means proven. It is reasonable, however, to suppose that the avoidance of overfeeding may obviate not only the obesity but incidentally a possible diabetes.

When we consider the active participation of the liver in the intermediate metabolism of fat, the development of biliary diseases in obesity is readily comprehensible. Appropriate feeding experiments show that the fats entering the body pass through the liver, become modified (hydrogenated) there, and then either undergo utilization or are deposited in the adipose tissues. On the other hand, in fasting or starvation, the fats are mobilized from their depots, carried to the liver and thence transported to various points in the body for utilization. Thus the liver is the central receiving and transmitting station both for exogenous and endogenous fats. In obesity the conditions appear to be particularly favorable for the development of biliary disorders. The incidence of cholelithiasis and other biliary diseases is, however, greater in women than in men, so that disorders of fat metabolism cannot alone be incriminated for the development of biliary disease, and factors incidental to the female sex must play a contributory if not provocative role. One fact in particular is worth mentioning in this connection, namely, that the occurrence or the recurrence of biliary disease is occasionally encountered in the course of reduction treatment for obesity. This too, is more frequently encountered in women than in men, and particularly when a rapid method of reduction is employed.

When gout was a more common malady than it is today, obesity was often associated with it, and prevailing opinion ascribed to the obesity an etiologic importance in the development of gout. While gout is by no means extinct, its

incidence, particularly in the arthritic form is rare. Atypical cases, in which a uric acid diathesis can be definitely established, are still encountered with some frequency, but its causal relation to obesity is by no means evident. There can be no doubt, however, that dietary indiscretions play an important part in the production both of gout and obesity, but certain other factors, usually adjudged to be constitutional, appear in the clinical picture.

It is also stated that obese individuals are particularly prone to infections, chief of which is pneumonia. This too is something which my own experience would lead me to question very seriously.

While obesity itself may promote sedentarism and thus aggravate pre-existing conditions such as orthopedic diseases, rheumatic states, cardiac disturbances, pulmonary tuberculosis, etc., it is plain also that such conditions require reduction of activity and favor sedentarism, and thus lay the foundation for the development of obesity. These conditions should, properly speaking, not be regarded as complications of obesity but as diseases frequently complicated by obesity.

Much or little can be said concerning the prognosis of obesity. We are still too uncertain as to whether obesity represents a disease, or merely an exaggerated physiologic condition. It may develop as a sequel to disease or may in itself be the precursor of definite pathologic developments. In either instance the outcome depends primarily upon the associated disease. The most that can be said is that obesity lessens the chances for recovery in any condition and must be considered as a serious element in every prognostic appraisal. Existing per se, and uncomplicated by other conditions, obesity offers no rules for guidance as to prognosis.

A great variety of methods have been introduced in the treatment of obesity, some of them on reasonable grounds and others not. Before discussing these methods, it is

well to consider first, the indications; how the degree of obesity can be appraised, and how far one should proceed. From the standpoint of indications, men and women present somewhat different problems. Reduction methods are often instituted, promoted by fashion or vanity, and not by the exigencies of hygiene or good health. In men, as well as in women, the indications for reduction should not be gauged exclusively by the accepted standards of normality in weight. Good health should be the first consideration. The presence of hereditary or familial trends in the history of pathologic manifestations as well as the age of the patient should all weigh in the final objective.

Generally speaking the older the individual, the less desirable does reduction of weight become, particularly if the obesity is not extreme, and if no clinical manifestations exist which would be benefited by loss of weight. It is only when pathologic developments occur or, when the weight itself is a hindrance in the exercise of normal activities and functions, that reduction should be considered.

It has been pointed out that vital statistics ascribe a higher mortality from all causes to the obese, but definite information is still lacking as to whether or not reduction of obese individuals is effective in actually prolonging their life beyond the usual period of expectancy. A close approximation of the ideal weight of an individual is obtained from standard tables. It has been observed in the study of such tabulations that a certain fairly constant numerical relationship exists between the skeletal dimensions and the weight factor; this has led to the evolution of a number of formulae for the computation of the ideal weight. The simplest of these is the one suggested by Moritz; the height of an individual is determined in centimeters. The number of centimeters over and above 100 is translated into kilograms and approximates the ideal weight. This formula has certain limitations, but it is of sufficient accuracy for clinical application. A variation of 10 per cent either way is regarded as normal, but surpluses greater than 10 per cent must be regarded as constituting obesity.

Efforts to control obesity date back many years, but the treatment of obesity has not received the earnest consideration from the profession that it deserves. Lukewarm interest and relative indifference have always characterized the doctor's attitude toward the subject; consequently the treatment of obesity has become grossly vulgarized, so that ultimately most obese individuals, particularly women, become the prey of commercial and other unscrupulous exploitation. Each day brings forth some new method of treatment or new device for reduction of weight, or at least an old one in a new guise.

Attention has been drawn to the pathogenic potentialities of obesity, and it is on their account that obesity becomes a pressing problem in preventive and palliative medicine. We have defined obesity as a condition in which an increment in weight follows when food intake exceeds energy output. It has also been indicated that in most instances the process is reversible. The main object of all forms of treatment is, therefore, a reversal of the conditions which lead to obesity, i.e., either a reduction in the food intake below the usual energy output, or an increase in energy output over the customary food intake, or both. When the customary intake of food becomes relatively excessive by reasons of decreased physical activity, then either the activity must be increased, or the diet reduced to the new level of nutritional requirement.

The most important problems in treatment relate, however to the already existing obesity. The question resolves itself into two phases: first, the treatment of those obese persons who show no complications and are otherwise well, and secondly those in whom obesity is a concomitant of some other disease.

The desired result in all these cases is a utilization of the stored fat as a source of energy. When the exogenous source of supply becomes reduced or depleted and the energy output remains the same, utilization of stored fat

occurs. Thus in the treatment of all forms of obesity reduction of diet is of primary importance. This is capable of great variation both qualitatively and quantitatively. The quantity of food restriction in any given case may be small or great and in some instances, may even border on starvation. The amount of restriction must vary according to the degree and the urgency of the result desired. Students of obesity generally agree that diets with a caloric value considerably below the basal requirement are the most efficacious in producing a prompt result. The degree of reduction sought is based, either on a foreknowledge of the weight of the patient prior to the development of the obesity, or the ideal weight for the individual, arrived at by means of the computations mentioned above. The time interval in which the reduction is to be obtained frequently determines the rigidity of the measures to be employed.

The caloric value of most modern reducing diets ranges between 800 and 1500 calories; some observers go considerably below this value, allowing only from 400-600 calories per day. However, the caloric value of the diet is not the only factor to be considered. The incidental and specific effects of the various food stuffs must be taken into account. Nitrogen loss does not ordinarily occur even after long periods of undernutrition, and tissue waste is readily guarded against by the administration of a basal amount of protein in the diet; about 0.6 to 1. gm. per kgm. body weight. On account of the specific dynamic action of protein which speeds up all the metabolic processes, diets containing much larger amounts of protein have been used with some success in reducing weight. On occasions a certain degree of debility may be experienced, particularly by young people during treatment; this is ascribable largely to the development of a moderate ketosis. A larger provision in carbohydrate intake serves to obviate this development. If marked undernutrition becomes necessary and treatment is protracted, provision must be made for an adequate supply of vitamine.

To describe a specific diet would be out of place, as a great variety of food combinations are possible. In any reduction diet it is important to give adequate amounts of protein, especially in the treatment of older individuals in whom physical deterioration must be guarded against.

Another very important factor in the loss of weight is the retention of water; it has been estimated that 1 gm. of carbohydrate causes from 3-5 gms. of water to be retained in the body, so that in order to effect the desired loss of weight, the carbohydrate intake must be redneed to a minimum. This may be accomplished by allowing approximately 0.8 gm. of carbohydrate per kgm. body weight. The combustion of the stored fat is accomplished by the generation of a large amount of water. It was pointed out earlier in the discussion that water retention constitutes a large part of the weight factor in obesity, and regardless of any theoretical considerations, it is a well known fact that obese people may fail to lose weight for a number of days even though they are undernourished. This is due to water retention. So that in observing the clinical effects of reducing diets, the influence of water must not be overlooked. It has been shown that under strictly controlled conditions, as much as 62 per cent of the loss of weight may be due to water. Mobilization of water is necessary for the successful reduction of weight. To that end a number of procedures have been devised, such as the administration of thyroid, salyrgan or neptal, calcium and other diuretics. The effect of these procedures is sometimes beneficial. It is important to remember in this connection, that the retention of water in obesity is frequently an expression of circulatory incompetency and attention must be given to that mechanism; it will be referred to again later. Experience teaches that when the outflow of water is not commensurate with the metabolic processes induced by undernutrition, the loss of weight is neither adequate nor enduring.

It was stated before that the treatment of obesity consists largely in a reversal of the conditions which cause

it; namely making the food intake less than the energy output, raising the energy output over the food intake, or both. We have already considered the first; now we come to the question of energy output. When the diet is properly adjusted the acceleration of the metabolic processes is accompanied by the combustion and utilization of body fat. Two methods are available to accomplish this. The first is increased physical activity through exercise, and the other is direct stimulation of the metabolic processes by medicinal means. Exercise increases the oxidative processes in the body, thereby accelerating energy output. Increased loss of water also takes place. But, exercise for the purpose of working off fat is merely a stimulant to the appetite. Unless accompanied by food restriction, its employment in the treatment of obesity is of questionable effectiveness.

Medicinal agents are frequently resorted to in the treatment of obesity. Chief amongst these is thyroid or thyroxin, thyractin, and recently dinitrophenol. Foreign proteins as milk or aolan have also been used. The purpose in the use of all of these is to increase tissue activity and hence the combustion of fat. Because of its effect upon metabolism, thyroid has always been regarded as a desirable adjuvant in the treatment of obesity. The popularity of all of these agents is based upon the misconception that they do away with the need for dietary restriction. But, experience teaches that barring those cases of obesity which are directly traceable to thyroid hypofunction, its usefulness is extremely limited. It is a remarkable fact, that whereas in the truly hypothyroid obesities, the amount of the hormone necessary to produce a definite effect is relatively small, in most other cases very large doses are necessary to produce a noteworthy effect. This is frequently achieved only at the expense of the patient's health, for the reason that in the obese person the thyroid is in all probability already subject to a definite functional strain.

To present the picture graphically, the obese individual may be conceived as possessing two bodies; an outer one consisting of adipose tissue which is relatively inactive, and an inner one made up of all the other tissues of the body which are metabolically active. We know that the basal metabolism is usually normal in obesity; that signifies that the inner body or the active tissues must work at a greater speed in order to maintain the metabolism at that level, than it does in the normal individual. The degree to which the metabolism of this inner body must rise is proportionate to the surface area due to the obesity. The increased rate of activity is presumably due to overactivity of the thyroid. From this it becomes obvious that the administration of thyroid in the treatment of obesity is a somewhat hazardous procedure, and as mentioned before, may be accompanied by toxic symptoms. I have found from experience that the untoward effects of thyroid therapy may be considerably diminished by the addition of small doses of iodine, and that much larger doses of thyroid can be tolerated if iodine is given at the same time. The other agents which I have mentioned such as the injection of foreign proteins, stimulate tissue activity through their pyrogenic properties. Dinitrophenol in small doses augments all the metabolic functions resulting in a steady loss of weight; in larger doses it produces a hyperpyrexia. However, it is too new a remedy to be used with any freedom and is capable of causing toxic manifestations. At best the results produced by pyrogenic agents are too brief to be of lasting value, unless a process of progressive tissue disintegration is induced by these substances.

It may be said therefore, that because of the physiologic strain which obesity throws on the organism, as evidenced by the high level of metabolism of the active tissues, thyroid extract and other agents which increase the total energy output are generally contra-indicated. From observations on large numbers of obese individuals, it has been found that only very few, not over 2 per cent, do not lose

weight on diet alone. These patients cannot be differentiated from the others. either by history or physical examination; they may sometimes be recognized after careful observations of the rate of weight loss and of the basal metabolic rate during a period of dieting.

The beneficial effects of dietotherapy may be ascribed to the drop in metabolic rate which follows upon moderate restriction of diet. Excess fatty tissue alone is removed and accounts for the feeling of well being and increased resistance to fatigue observed in individuals so treated. It is well to remember that the dietary treatment of obesity is still the most important and satisfactory therapeutic method, and cannot be replaced by medicinal agents.

When obesity is complicated by pathologic conditions the principles of treatment remain virtually the same. Undernutrition is the method of choice in all instances except those associated with diseases of the biliary passages; here the procedure must be slow. In diabetes, as Allen has long ago pointed out, undernutrition is the ideal method of desugarization; and on account of the frequent association of obesity with diabetes, reduction of weight is accomplished at the same time by this means. In cardiac and circulatory diseases restricted food intake is of the utmost importance. Its beneficial effects are traceable to many influences; chief of which is unquestionably the reduction in the basal metabolism. The influence of this factor on the circulatory system has come to be appreciated only since the recent work of Blumgart referred to earlier in the discussion. It relieves the physiologic strain caused by the obesity on the metabolism. Combustion of body fat and removal of retained water add to the effectiveness of undernutrition. As the digestive functions in such cases are more often impaired than not, the administration of the Karrel diet is a simple and suitable way of accomplishing the desired result. It is in this group of cases, where prompt elimination of retained water is so desirable that the employment of diuretic agents such as salyrgan or neptal, calcium, etc. are particularly useful.

To summarize then, obesity is a condition which results from the exaggeration of a physiologic process and culminates in the accumulation of excess fat. The chief factor in this process is the inequality between food intake and energy output. In certain instances, disease of the central nervous system or dysfunction of the endocrine glands so affects the metabolism of the body as to favor and accelerate the generalized or localized deposition of fat. In close association therewith, water is retained in the tissues. The joint effect of the accumulation of fat and water may be detrimental to the efficiency of the circulatory apparatus, may affect the activity of the endocrine glands and impair the functions of the liver and pancreas, leading to other diseases. It may further undermine the vitality of the whole body so as to render it susceptible to a variety of accidents.

The rational treatment of obesity is based upon the reversal of the physiological process which leads to the deposition of fat. It aims to reestablish a balance between the output of energy and the intake of food. The aid derived from the use of medicinal agents is directed largely toward the acceleration of metabolism and the elimination of water; these measures appear necessary in a restricted number of cases and are at best, of limited effectiveness.

A CRITICAL ESTIMATE OF THE VALUE OF LABORATORY PROCEDURES IN DISORDERS OF METABOLISM*

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If I had chosen the title for this talk I should be guilty of presumptuous arrogance. As your entertainment committee wished it upon me, I can only feel flattered that they should have believed me capable of condensing such a subject into 45 or 50 minutes, especially after I had recently displayed my incapacity by expending on the same subject, with my friend Van Slyke, some 1200 pages of rather fine type. I pity you for the disappointment that is in store for you and may as well confess that I have substituted for the expected abstract, which is clearly beyond my powers, some general reflections on the place of the chemical analysis of blood in medicine which have only the weight of my personal opinions unless the practical illustrations which I shall offer may lend them some interest and conviction.

It is hard to believe that in this subject almost the whole of the great mass of literature and knowledge (the two are quite distinct) has been developed in the course of two decades, since Bang, Folin, Van Slyke, Benedict and others presented to the physician, at just the moment when venous puncture was becoming a common procedure, practical methods for the analysis of blood. These methods, born in the physiological and chemical laboratories were put into the hands of clinicians who had neither the analytical training to utilize them, nor the physiological and chemical education necessary for their interpretation. This is not said entirely in a spirit of criticism; because there is reason to be proud that clinicians have been found with critical judgment and industry great enough to overcome these initial handicaps. Their contributions have not

* Delivered October 31, 1933.

been confined to pathology, but have extended back to the mother sciences of physiology and chemistry. Nevertheless, this knowledge was secured by the noblest only after false steps. Furthermore, as in all virgin fields, no step of any kind could be taken without the discovery of something new and these discoveries came in such confusing profusion that it was impossible to take time to separate gold from dross. The great mass of exploiters, trained in a purely clinical field and reasoning in the usual simple and direct manner, that no two things can coexist without being related, immediately began to connect chemical abnormalities with specific diseases, without consideration of the fact that physiology deals with functional disturbances and cuts along other lines than pathology. Too many of these conclusions reached in the first heyday of excited exploration have received the unmerited sanction of tradition and threaten to be transmitted as part of accepted medical lore to the next generation, which deserves better at our hands.

It is, perhaps, deplorable that clinical chemistry sprang into active life during the period of therapeutic nihilism when medicine felt its duty done if it gave the patient a name to die by, perhaps illuminating it with a placebo. This spirit only exaggerated the tendency mentioned above, to connect diseases with chemical abnormalities and, for a long time, diverted attention from what is at least as important an aim of physiological chemistry, the logical direction and control of the treatment of the disorder which the analyst has revealed. The clinician, meantime, was provided with his chemical tools only one at a time—to be sure in such rapid succession that he had not time to perfect himself in the use of one before the next appeared. Nevertheless those which custom had made first familiar received a lasting preference which has given them undue authority to the exclusion of others. The continuous appearance of new models of old techniques made selection even more difficult. As these new models were frequently simplifications and not improvements, preference was too often given to inferior procedures.

Technical complexities of procedure and the special knowledge required for proper interpretation has had its usual effect in segregating a province of medicine. There is no escaping the necessity of therapeutic specialization; it is, however, regrettable that this leads to restriction of vision by separation along artificial lines. The term "diseases of metabolism" implies a most unfortunate line of separation. I may say that the only change I was permitted in my title was the substitution for this opprobrious epithet of the term, "disorders of metabolism". From the therapeutic standpoint the treatment of diabetes, nephritis and certain endocrine disorders requires more experience and special knowledge than that in the possession of most practitioners. More important is the fact that to conduct such treatment in an efficient and economical manner necessitates a prohibitive expenditure of time and effort unless there is enough work to warrant the maintenance of a certain amount of special organization and machinery. Specialization on the basis of techniques is, however, dangerous, whether the technique be that of electrocardiography, roentgenology, or chemistry, if the specialist loses sight of the general problems of physiology and pathology or the general practitioner becomes unable to evaluate the special examinations. Nothing but evil can come of a situation in which the discovery of glycosuria by the practitioner is the signal for a diagnosis of diabetes and a note to a metabolism clinic; although this may be preferable to retention of the patient and unintelligent treatment. If, on his part, the expert has become so narrowed in his outlook that he allows the patient to die of tuberculosis in behalf of diabetes, his value to medicine is somewhat fictitious.

This is, however, a small issue compared with the fact that a few particular diseases which manifest themselves chiefly in disturbances of metabolism have come to be considered the peculiar province of the metabolic specialist and his techniques. This division has deprived the general clinic of the benefits of one great branch of physiological

knowledge, has restricted the machinery for the investigation of metabolic disorders and has robbed the specialist in his corner of the advantages that would come from wider comparison and analogy. This leads inevitably to the treatment of diseases rather than patients. There are no diseases of metabolism. There are no diseases that are not attended by disorders of metabolism, because metabolism is the sum of those processes by which life and its functions are maintained. There is no reason to believe that rectification of these disorders is superfluous because the disturbances do not dominate the picture, because they are not detectable by conventional routine procedures, or because their treatment does not strike at the fundamental cause of the disease. After all, diabetes itself can at this moment be looked upon only as a symptom complex and, insulin to the contrary notwithstanding, is treated only by palliative, symptomatic methods.

My plea, then, is not for less chemistry, whether it is measured in procedures or their application, but for more chemistry, and better chemistry, more widely and thoughtfully employed. I should like multiplication rather than restriction of procedures with careful selection in each case of those best adapted to give the most useful information, not the endless repetition in all patients of some especial "blood chemistry routine", too often chosen because it fits some system of blood analysis devised for the convenience of the analyst. Finally I would have the chemical data examined and interpreted, not as things apart, but with due recognition of all other available information. Nor should the scope of examination along any other relevant line be limited by the fact that a metabolic disorder dominates the clinical picture.

The common statement, that a chemical procedure is good enough for clinical purposes should arouse suspicion at once. First of all, it implies that selection has been determined by the convenience of the technician with the patient as a secondary consideration. Moreover, it suggests a carelessness of attitude that engenders feelings of un-

Table 1. The distribution of chemical substances between cells and serum and the effects of cell volume on whole blood analysis. The data are collected from various sources, many from data secured in the author's laboratory (See footnotes, following page).

Substance	Standard of Measurement	Plasma	Cells	Whole Blood	
				Normal[1]	Anemic[2]
Total protein	per cent (N × 6.25)	7.0	35.0	19.5	15.2
Hemoglobin	per cent	0	35.0	15.6	8.4
Serum albumin	per cent	5.0	0	2.8	3.9
Serum globulin	per cent	2.0	0	0.9	1.6
Total non-protein nitrogen	mg. per cent	29	49	39	33
Urea nitrogen	mg. per cent	19	17	18	18
Uric acid[3]	mg. per cent	3	3	3	3
Creatinine[4]	mg. per cent	1.2	1.2	1.2	1.2
Creatine	mg. per cent	0	6	2.7	1.4
Amino acid nitrogen	mg. per cent	6	10	7.8	6.9
Glucose[5]	mg. per cent	96	75	86	91
Sodium	mg. per cent	310	+[6]	172+	241+
Potassium	mg. per cent	18	420	197	107
Calcium	mg. per cent	10	0	5.6	7.8
Magnesium	mg. per cent	2	5	3.4	2.8
Bicarbonate	CO_2 content (vol. per cent)	68	45	58	63
Chloride	mg. per cent	362	192	285	323
Inorganic phosphate[7]	mg. per cent of P	3	3	3	3
Organic phosphate	mg. per cent of P	0.5	52	24	12
Fat	mg. per cent of fatty acids as tripalmitin	355	?[8]	?	?
Lipoid phosphates	mg. per cent of P	9	16	12	11
Cholesterol	mg. per cent	207	?[8]	?	?

certainty. Surely nothing is to be gained by straining at chemical gnats and swallowing clinical camels. But medicine has quite as much dignity as the other biological sciences and it behooves the clinician to treat it with due respect himself and to resent any slurs that may be cast upon it by snobbish chemical confreres. Not only must the clinician assure himself that a chosen technique is capable of the desired accuracy, but he must assure himself that it is being applied, with adequate controls, by persons who are proficient enough to secure this accuracy. His duty does not, however, cease at this point. It is a waste of time and effort to strain for analytical accuracy on unsuitable material. The aim of clinical chemistry is to gain information concerning disorders of life processes, not *post mortem* changes. In blood, shortly after it is drawn, glucose begins to decompose, with formation of lactic acid; the organic and inorganic phosphates may undergo certain permutations; nitrogenous compounds are broken down by the action of bacteria and enzymes. All of these changes are retarded by keeping blood cold, sterile and out of contact with air; some can be prevented by the use of preservatives of the proper kind. But these measures are only palliative; the only true corrective is to reduce to an absolute minimum the interval between collection and analysis of blood.

For certain analyses only serum or plasma can serve; blood is useless. This is especially true of inorganic analyses. The reasons will be obvious from Table 1. In

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[1]Oxygen capacity 20.9 vol. per cent (15.6 gm. per cent hemoglobin), cell volume 44.5 per cent.

[2]Oxygen capacity 10.45 per cent (7.8 gm. per cent hemoglobin). cell volume 22.25 per cent.

[3]Uric acid values and distribution are somewhat uncertain.

[4]The distribution of creatinine is not entirely certain.

[5]These figures are from Somogyi and represent true glucose. Cells contain larger amounts of reducing substances other than glucose. Therefore analyses by the usual methods indicate a somewhat different distribution.

[6]It has been assumed that the cells are free from sodium, but they may contain minute amounts of this element.

[7]By inorganic phosphate is meant total acid soluble phosphates — inorganic phosphates, i.e., phosphate esters.

[8]The distribution of fatty acids between cells and plasma is still uncertain.

this table the first two columns show the distribution of a variety of substances between cells and serum of average normal blood, the third column, the concentrations of the same substances in whole blood. The fourth column represents the effects on whole blood of reducing the cells 50 per cent (that is, producing an anemia) while the concentrations of all substances in serum and in cells remain the same. It is at once evident from the table that about those substances which are most unevenly distributed whole blood analyses can give no useful information. From examinations of whole blood it would seem that chloride, sodium and bicarbonate were increased and calcium, potassium and creatine diminished in all patients with anemia, although the concentrations of these substances in both cells and serum are entirely normal.

When blood is exposed to air it loses carbon dioxide and takes up oxygen. Simultaneously the cells contract somewhat, yielding water to the plasma. Therefore, if the chemical constitution of serum is to be determined, strict accuracy demands that the blood be taken, preserved and centrifuged without contact with air. This is of the greatest importance if knowledge of its CO_2 content is desired; however, neglect of these precautions may introduce an error of no negligible magnitude in the determination of cell volume, chloride, proteins and sodium. Certainly, if serum analyses are contemplated, more than the usual care must be taken to prevent decomposition of blood and to expedite analysis. Errors due to air exposure are small compared with those that result if any degree of hemolysis is produced by careless handling. Furthermore, anticoagulants can not be employed with impunity because they may also alter the volume of the blood cells. The use of serum, rather than plasma, for analyses has much to recommend it. Personally I believe that more useful information could be secured if, in spite of the additional trouble involved, serum was rather widely substituted for whole blood. Such an expedient as the new Folin method of securing so-called "unlaked blood" filtrates has too many elements of uncertainty and is, at

best, limited in its application. The point I wish to emphasize, however, is that the physician who sends blood for chemical examination must know, not only what analyses may be of advantage, but also enough about the technique of drawing and preserving blood to avoid prejudicing all the efforts of the chemist. A word may be added concerning the technique of venipuncture. In conditions of venous stasis fluid passes out of the blood stream into the tissues. If venous obstruction is maintained for 5 or 10 minutes as much as 10 per cent or even more of the water may escape from blood and this change is accompanied by disturbances in the concentration of most of the chemical constituents of the blood. Analyses of samples collected under these circumstances can give only a sorry impression of the actual composition of blood circulating in the vessels of the patient.

Of the substances listed in Table 1, which is far from complete, the average physician confines his interest to three or four constituents. Hemoglobin is, of course, relegated to the non-chemical technique of the clinical pathologist. Serum proteins and their fractions, albumin and globulin, are only beginning to become popular in the classification of nephritis, while their value for other purposes is little appreciated. Loss of protein into the urine is not the only condition which depletes serum albumin. This fraction of the proteins diminishes in all conditions of malnutrition (protein starvation) and, when for this reason it falls below a certain level, edema as surely appears as it does in nephritis when a comparable reduction of albumin results from proteinuria. Moreover, in malnutrition, as in nephritis, it is the albumin fraction which suffers. Diagnosis in cases of edema of obscure origin would be measurably advanced by more frequent serum albumin determinations and the physician would regard with less equanimity the discomforts of a patient on a diet containing insufficient protein if a report of low serum albumin gave him objective evidence that the subject was starving. During the treatment of diabetic acidosis it is quite unfashionable to omit determinations of blood sugar and carbon

dioxide. Yet there is much evidence that neither hyperglycemia nor acidosis is of such imminent importance as the dehydration and concentration of the blood that accompany this condition and finally lead to fatal shock. I do not wish to disparage the value of sugar and carbon dioxide determinations; but would add some measure of the water content of the blood. For this purpose, repeated estimations of hemoglobin may serve, but determination of serum proteins is superior. It is even more useful in estimating the effects of fluid administration in other more chronic dehydrating conditions. And may I add, without offense to the cardiologists, that under the most meticulous chemical guidance the clinician is not relieved of the necessity, even in diabetic acidosis, of observing with watchful care the state of the peripheral circulation, and especially the blood pressure, which gives the most reliable and earliest warning of the onset of shock.

Serum globulin reacts to quite other influences. It is little reduced by albuminuria and nutritional disturbances, unless these are caused or attended by infections. It is found elevated in most infectious diseases, especially if there are extensive ulcerations or suppurative processes. Tuberculous or syphilitic ulcerative conditions appear to have a particularly striking effect. In kala azar extremely high values are observed and are the basis for Ray's hemolytic diagnostic test for this disease. The disease in which it may reach the greatest heights, however, is multiple myeloma. The association of extreme globulinemia with anemia and rarefaction of the bones may establish the diagnosis of myelomatosis in a patient who fails to excrete Bence-Jones protein in the urine. Such a case in our own clinic had been given a diagnosis of hyperparathyroidism because of the presence of extremely high calcium and low phosphorus in the serum and a negative calcium balance. The discovery of 9 per cent of globulin in the serum, instead of the usual 1.5 to 2.5, established the diagnosis which was confirmed at autopsy, when the parathyroid glands were also found to be entirely normal. Obviously determinations of serum proteins and their fractions

should not become part of a routine chemical system indiscriminately applied, but may give information of great value for diagnosis and the direction of treatment, if they are employed with discernment.

About non-protein nitrogenous constituents, since the pioneer articles of Folin and the early work of Myers, has developed a tradition that leads to unnecessary work in the routine determination of nitrogen partitions. In general, urea makes up so large a fraction of the total non-protein nitrogen that it is almost a matter of indifference which of the two is chosen, unless determination of the urea clearance is intended. If serum proteins are to be measured at the same time the total non-protein nitrogen must be determined any way and urea is more or less superfluous. Only in the last hours of diseases with profound liver damage is any information of advantage secured by measuring both non-protein nitrogen and urea. In these conditions, when the liver is no longer capable of breaking up the amino acids and the kidneys are incapacitated, the blood urea may be found normal or low, while non-protein nitrogen is greatly elevated. In the present confused state of knowledge of uric acid and purine metabolism we are at a loss to explain abnormalities of blood uric acid. The reputation which this substance enjoyed in the diagnosis of renal disease is exploded. Even for the diagnosis of gout it has proved of little value because it is so frequently and inexplicably high in other conditions and may be normal in outspoken gout. On the other hand, this disease is so often accompanied by arteriosclerosis and kidney disease, that its victims deserve careful examination of renal function.

The concentration of creatinine is seldom increased unless there is grave kidney damage. For this reason, importance has been attached to it as a criterion of prognosis in nephritis. It is quite generally stated that if blood creatinine exceeds 5 mg. per cent early death may be expected. This is true only in chronic renal diseases. Higher values, found in severe acute nephritis or in surgi-

cal diseases of the kidney, are compatible with recovery. Because creatinine rises only in the terminal stages of chronic nephritis, when urea has reached high levels, its determination in mild or early nephritis or in forms of the disease which are not associated with nitrogen retention is superfluous. After all, prognosis is not the chief aim of medicine. Creatinine gives little indication of the efficacy of therapeutic measures. Attention should be called to the use of creatinine excretion as a measure of renal insufficiency. It is becoming increasingly popular, although it is still uncertain whether it has any advantages over some of the simpler tested methods. On the whole determination of creatinine is among the measures that should be employed only in selected cases, when blood non-protein nitrogen and urea are elevated.

The impression is altogether too wide-spread that high blood non-protein nitrogen or blood urea is pathognomonic of kidney disease. So far is this idea carried that the degree of nitrogen retention is frequently used as a measure of the severity of renal injury. No basis for such a concept can be found in physiology. The non-protein nitrogen content of the blood may be considered as the resultant of three factors: the rate of destruction of protein in the body, the concentrating powers of the kidneys and the amount of water excreted. If the destruction of nitrogen is great enough, as it may be in such profound intoxications as lobar pneumonia, the blood non-protein nitrogen may rise even when the kidneys are sound, especially if water excretion is small because the patient has received too little fluid. Such increases, even when they have attained considerable magnitude, may disappear overnight if the urine volume is augmented by the administration of more fluids. Persistent vomiting—for example, in pyloric stenosis—may so deplete body fluids that the urine becomes extremely scanty merely from lack of available water. High blood non-protein nitrogen results, and responds again to parenteral administration of fluids. In these circumstances nitrogen retention should be considered not as an indication of renal disease, but as evi-

dence of toxemia and dehydration and may serve as a warning. If, for any reason, in nephritis, the urine volume is reduced, or protein destruction exaggerated, a kidney which could, under favorable circumstances, perform its function in a satisfactory manner, may be unable to excrete enough nitrogen. Gastro-intestinal disturbances, febrile diseases, and heart failure are the conditions which most frequently bring about such states of renal decompensation. With the relief or disappearance of these complications the blood non-protein nitrogen may return to its normal level. On one occasion in my experience a stuporous state, anuria and a non-protein nitrogen of 321 mg. per cent led to an initial diagnosis of uremia, diverted therapeutic efforts, and delayed operation in a patient with pyloric obstruction who proved, at autopsy, to have normal kidneys. An old woman with generalized arteriosclerosis involving the kidneys, and congestive heart failure, had a blood non-protein nitrogen of 140 mg. per cent. With rest and digitalis this fell rapidly to normal limits and, just before she died from carcinoma of the rectum, 18 months later, was only 40 mg. per cent. These are only two of many examples that could be given of the fallacy of interpreting non-protein nitrogen in terms of renal pathology only, the dangers of drawing conclusions from single determinations, and the information concerning the efficacy of treatment that may be gained by frequent examination of the blood. It must be recognized that no one of the nitrogenous compounds of the blood rises in uncomplicated renal disease until kidney destruction is far advanced.

The difficulty involved in the preparation of blood serum as well as the actual chemical procedures employed, has restricted the determination of the inorganic constituents of blood largely to research laboratories. And yet no chemical properties of the body are more solicitously guarded or more important for the proper conduct of the vital functions than the concentration and pattern of salts in the body fluids. On these depend, among other things, the

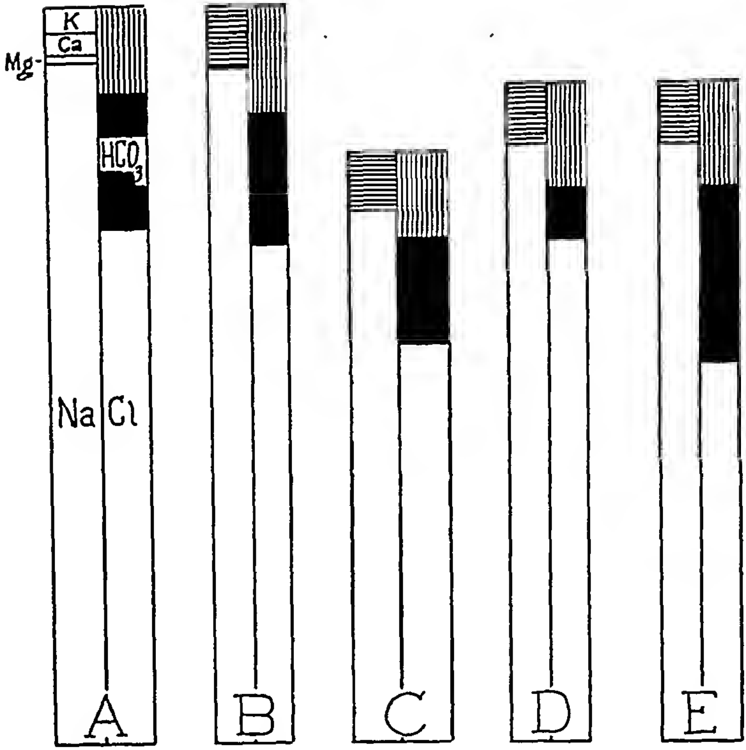

Fig. 1. Schematic representation of electrolyte patterns of the serum in conditions associated with dehydration. The concentration of electrolytes is indicated by the height of the columns, the volume of the body-fluids by their width. The unlabelled, vertically ruled segments represent the proteins, phosphates, sulfates and organic acids. Except in A the bases, K, Ca and Mg, have been treated as a single unit, horizontally ruled.

A. Normal average. B. Proportional reduction of water and salt. C. The result of restoring the water, but not the salt in condition B. D. and E. Loss of 1/5 of the volume of the body fluids and an extra 1/10 of the salts. In D the salt has been lost chiefly in the form of bicarbonate, in E, chiefly as chloride. The latter is the picture of pyloric obstruction or profuse vomiting of hydrochloric acid; D may be encountered in severe diarrheas.

maintenance of both osmotic and acid-base equilibria. Everyone in the audience is familiar with the fact that blood cells and other cells, when their normal environmental medium is diluted with water, swell and finally rupture. If they are diluted with an isotonic salt solution they neither swell nor rupture. In life dilution of the body fluids has deleterious effects which can probably be ascribed to phenomena of the same nature, although they do not usually proceed to the point of cell destruction. Administration of excessive water to animals produces symptoms of intoxication which may be fatal. That these are referable, not to expansion of the body fluids, but to dilution of salts in those fluids, can be inferred because administration of equal amounts of normal salt solution produces no symptoms and because, when symptoms have been provoked by water administration, they can be relieved by giving salt. If the salt supplies have been previously depleted less water is required to induce intoxication. This is illustrated by miner's or stoker's cramps. Miners and stokers who lose enormous amounts of salt by sweating during the performance of heavy labor at high temperatures, are prone to develop cramps when they slake their thirst with water. These symptoms can be prevented or relieved by the administration of salt. Undoubtedly water intoxication is not uncommonly provoked by physicians who, with the best intentions, employ water without salt to combat dehydration.

In Fig. 1, the two columns at the left illustrate schematically the composition of the salts found in the serum. In order that comparisons may be facilitated concentrations are given not in the conventional terms of mg. per cent, but in terms of combining equivalents (milliequivalents per liter, m.eq.), a usage which is becoming more and more general. (Let me remind those who find the term m.eq. strange, that it has the same significance as c.c. of 10th normal solution per 100 c.c., the conventional standard for the measurement of acidity of gastric contents and urine.)

In a medium so nearly neutral as blood serum the bases cannot differ appreciably from the acids. For this reason determination of the bases affords a measure of the total salt concentration in serum. Because sodium makes up such a large fraction of the total base, analysis for this element yields practically the same information. Conditions which cause dehydration invariably deplete the salts of body fluids, chiefly at the expense of sodium. Whether this salt depletion is demonstrable by blood analysis depends on the proportions of salt and water which are lost. Analyses of blood, unfortunately, give no information concerning the absolute quantity of any substance in the body, but only of its concentration. In the figure the difference is indicated by the two dimensions of the columns. Concentrations are represented by the height, the volume of the body fluids by the width of the various columns. For example, Figure 1 B, in which the columns are narrower by 1/5th, but the same height as those in A, illustrates a condition in which 20 per cent of the water of serum has been lost with an equivalent amount of salt. In spite of these great losses, beyond a slight increase of the proteins the chemical pattern of the serum is practically normal. C represents the result of restoring the water of the body, without salt. This is the condition in water intoxication. The actual deficiency of body salts in B and C is the same, but it is demonstrable by chemical analysis only in C. Usually in conditions of dehydration salts are lost somewhat in excess of water, yielding pictures like D and E. In both the fluid volume has been reduced 20 per cent, salt an additional 10 per cent. Confronted by such a situation, it is obviously necessary to give salt and water in amounts and proportions so adjusted that both the volume and the composition of the body fluids will be restored to normal. The quantities of salt and water required can not be estimated by any exact rule. In general, in addition to normal saline some extra water or glucose solution is usually needed to offset the continual slight dissipation of water without salt by the lungs and skin. Every effort must,

however, be made to restore body fluids without producing the water intoxication picture illustrated in C.

The ideal criteria for the evaluation of the degree of dehydration would be analysis of the serum for base or sodium and measurement of the body fluids. The latter is impossible. Imperfect information can be secured by serum protein or hemoglobin estimations; but these, at the best, only measure hemoconcentration, which is influenced not only by the volume of fluid in the body, but also by its distribution. Furthermore, hemoglobin and protein may have been affected by pre-existing anemia, or malnutrition. At present we must depend for the estimation of the state of the fluid supplies of the body upon clinical observation of the state of the mucous membranes, the elasticity of the skin, intraocular tension, the state of the circulation, etc. During treatment measurements of the base or sodium of serum would aid greatly in the regulation of fluids. Unfortunately, the procedures now available for the determination of total base or sodium require so much time that their practical utility is very small in the conditions of emergency for which they are most needed. If attention is turned for the moment to the acid columns of the figure it will be apparent that bicarbonate and chloride make up the great bulk of acid, with chloride predominating. Together they almost balance the sodium. It follows, as figures C, D and E indicate, that any important change of sodium will be reflected in the sum of bicarbonate plus chloride. Therefore, this sum may be used as a practical measure of the total base or sodium concentration of the serum.

Considering the relative simplicity of the procedures for the measurement of carbon dioxide and chloride and the frequency and seriousness of dehydration, it is both surprising and distressing that this combination of tests is not more generally employed in the clinic. It would be fair to say that there are few conditions in which the most satisfactory information can be secured by either test alone. Even in diabetic acidosis sodium and chloride are

depleted quite as much as bicarbonate—or more—and their restoration is quite as important. It may be well, for a moment, to consider a few of the common conditions attended by dehydration and salt depletion of clinical magnitude. One of these, diabetic acidosis has been twice mentioned already. In this condition, if shock is prevented and body fluid and salt restored, all the alarming symptoms may disappear while the blood sugar is still greatly elevated and serum bicarbonate reduced and while glycosuria and acetonuria persist.

Vomiting sacrifices both salts and water. Its effect on serum and other body fluids depends on the duration and severity of the vomiting and the nature of the vomitus. If the latter is highly acid a condition like that depicted in E results; chloride becomes especially depleted, while bicarbonate may be normal or high. Sodium and water always suffer and, if the vomiting has been sufficiently severe and prolonged, the loss of sodium usually exceeds that of water. This becomes evident in the serum in reduction of the sum of bicarbonate and chloride. Determination of these two substances may aid in establishing a rapid diagnosis of the nature and severity of the vomiting. In functional gastro-intestinal disturbances or psychoneurotic vomiting the chemical pattern of the serum is less often disturbed because, despite appearances, patients with these conditions usually retain enough food and fluids to escape serious dehydration and salt depletion. However, as usual, chemical examination of the blood is more important as a guide to therapy than as an aid to diagnosis. In organic obstruction of the intestinal tract operative interference is far better tolerated if dehydration is first overcome and the salt content of the body fluids restored. Subcutaneous or intravenous administration of large amounts of sodium chloride and glucose solutions should precede operation. In the treatment of peritonitis or paralytic ileus the same treatment is indicated. The efficacy of these measures can well be checked at frequent intervals by chemical examination of the serum to

learn whether the proportions of salt and water have been well chosen.

The dehydrating and salt-impoverishing effects of diarrhea have been recognized since Carl Schmidt published his famous monograph on epidemic cholera in the middle of the last century. They have, however, received too little therapeutic recognition outside of the field of pediatrics.

Loeb has recently pointed out that the most striking and consistent disturbance of metabolism in Addison's disease is reduction of the sodium concentration of the serum. In the absence of the suprarenal glands the kidneys apparently allow sodium salts to escape in excessive amounts into the urine. During the acute crises of the disease the sodium of the serum is low and symptoms may be alleviated by the administration of large amounts of salt. During the more chronic stages the concentration of sodium in the serum may be normal; but if salt is withdrawn from the diet, rapidly falls to a subnormal level. This effect of salt restriction on serum sodium (or bicarbonate and chloride) may prove an aid in the diagnosis of Addison's disease; but must be checked by frequent analyses of serum, because, if the restriction is prolonged too far a serious crisis may be precipitated.

In lobar pneumonia and other acute febrile diseases, if insufficient fluids and salt are given, sodium and chloride are also wasted and their concentrations in serum fall. Here again the regulatory powers of the kidney appear to be lost and care should be taken to provide enough salt in the diet to replace the wastage.

If the circulatory and renal systems are competent, and sufficient absolute amounts of salt and fluid are given to satisfy the requirements of the organism, the kidneys will make the necessary finer adjustments by excreting any excess of water or salt or even individual ions. For example, in the vomiting of pyloric obstruction there is sacrificed more chloride than sodium. Apparently the most efficacious treatment, if it were feasible, would be the

administration of hydrochloric acid in addition to sodium chloride. However, if enough fluid and sodium chloride are given to induce a free flow of urine the kidneys will excrete more sodium than chloride, thus restoring the normal electrolyte pattern of the serum. If, on the other hand, insufficient amounts of salt and fluid are given or the kidneys are not competent, such secondary adjustment is impossible and both the quantities of fluid and salt given and the nature of the salts must be regulated with the greatest care. Under these circumstances, especially, the concentrations of bicarbonate and chloride in the serum must be watched with the greatest care and frequency if the patient is to receive therapeutic justice. The simple excretory function of the kidney has been too much stressed, the selective discrimination with which it is exercised has received little thought. Uremia is generally looked upon as an intoxication resulting from the retention of excretory products, although an equally good brief could probably be prepared for the theory that it is due to wastage of materials through incompetent kidneys.

The only definite and consistent result of reduction of renal substance is the passage of dilute urine, usually in uncommonly large amounts, loss of concentrating power on the part of the kidneys. Apparently the urine becomes more like a simple filtrate of serum. Those solutes, like the nitrogenous constituents, which are usually excreted in high concentration are less efficiently eliminated, while solutes, like sodium and chloride, which usually appear in lower concentration in urine than in blood, are now more highly concentrated and, therefore, wasted. The acidosis of nephritis is due less to accumulation of foreign acids in the blood than it is to excessive loss of the base, sodium. Dehydration and salt depletion are regularly found in terminal stages of renal disease, although the former is often masked by the presence of edema due to heart failure. The inability to prevent salt wastage is well illustrated by the course of the case depicted in Figure 2. The patient, a male, 42 years old, was admitted with hyper-

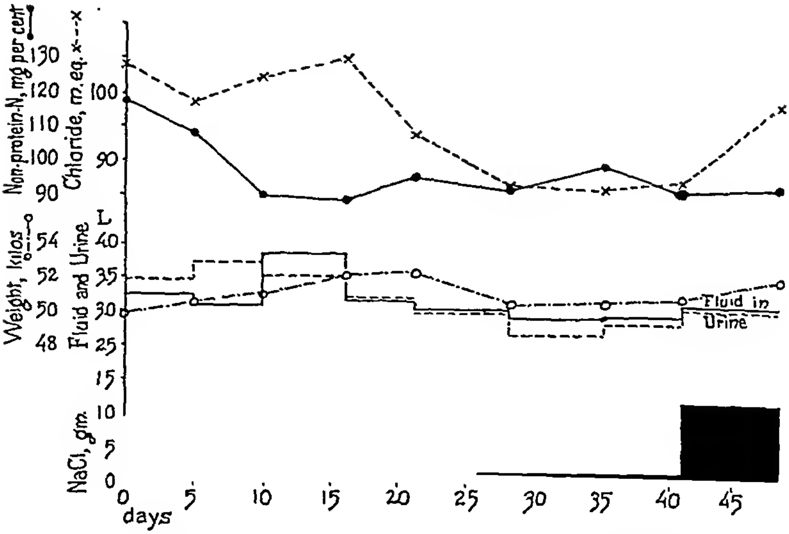

Fig. 2. The effect of varying salt in the diet of a patient with renal insufficiency. In the top section are represented the course of the non-protein nitrogen of the blood and the chloride of the serum; in the middle section, the obvious fluid ingested, the urine volume and the body weight; in the bottom section, the sodium chloride of the diet. On the 25th day the concentration of total base in the serum was only 126 m.eq.

tension, hypertrophy of the heart, irregularities, murmurs and electrocardiographic signs that suggested rheumatic or coronary heart disease, a urine of low specific gravity, with moderate amounts of albumin, red and white blood cells and casts, a phenolsulfonphthalein excretion of 16 per cent in 2 hours and a blood non-protein nitrogen of 96 mg. per cent, rising to 131 mg. after diuresis. The edema largely disappeared under the influence of rest and digitalis, but the blood non-protein nitrogen was little affected, although the urine volume was nearly 3000 c.c. per day. In the figure the black columns at the bottom indicate the quantities of chloride (as sodium chloride) which he received, the lines in the upper section represent the concentrations of non-protein nitrogen and chloride in the serum. In the middle are shown the weight, the intake of obvious fluid and the urine volume. The reduction of serum chloride under the influence of salt restriction is quite as great as one would expect in pyloric obstruction.

But, whereas in the latter condition far before chloride had fallen to this level in the serum, it would have disappeared from the urine, in the nephritic it continues to be excreted. It is also worthy of note that on 15 gm. of

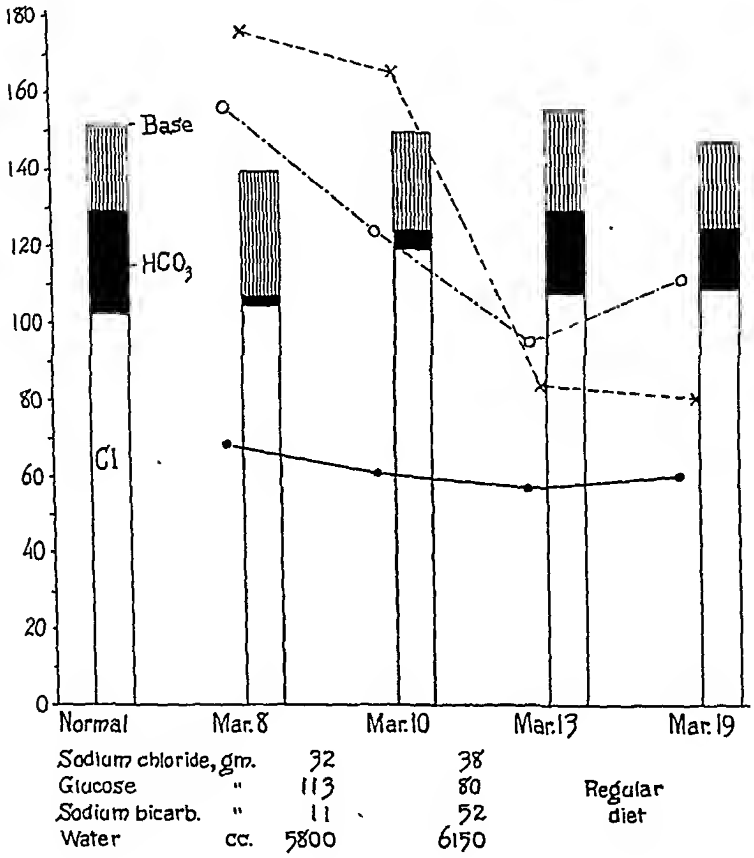

Fig. 3. The concentration of electrolytes in the serum of a patient with nephritis who had become dehydrated by vomiting. The concentration of total base is indicated by the total height of each column, the vertically hatched areas represent protein, phosphate, sulfate, and organic acid. The normal electrolyte pattern is shown, for comparison, on the left. All electrolyte values are given in m.eq. x — — — x = non-protein nitrogen of blood in mg. per cent. •———• = serum proteins in gm. per liter. o—·—o = hemoglobin in terms of volumes per liter of oxygen capacity. The treatment is indicated below.

sodium chloride a day, although there was some retention of chloride and water, edema did not appear and the blood non-protein nitrogen fell. Determination of total base, when chloride had fallen to the lowest point, showed that sodium was wasted with chloride.

Although, in this case, it is impossible to connect the fall of non-protein nitrogen with the high salt regime, there is some evidence to suggest that salt depletion may be connected with nitrogen retention. This has caused certain members of the French school to speak of nitrogen retention from lack of salt. This implies a relation of cause and effect that is hardly warranted by the facts. However, attention may well be called to the fact demonstrated by Loeb and verified by Harrop, that blood non-protein nitrogen rises as serum sodium falls during the development of the acute crises of Addison's disease, while there is profuse diuresis.

A more striking instance of dehydration and salt depletion and the difficulties of adjusting the chemical pattern of the serum was presented in a review of salt and water metabolism some years ago. The patient, a man of 58, who for 26 years, following a fracture of the spine had suffered from incontinence of urine, was seen in consultation after spontaneous rupture of a perineal abscess had resulted in a urethral fistula which had been drained by operation about 12 days earlier. At this time he appeared greatly dehydrated, comatose, and his respirations were exaggerated. The serum electrolytes, the therapy which was practised and its results are shown in Figure 3. Again normal concentrations are indicated in the columns at the left of the figure. At the onset base, chloride and bicarbonate were all extremely reduced. After 2 days, during which he received large amounts of fluid, glucose, and sodium chloride, and some sodium bicarbonate, intravenously and subcutaneously, base had risen almost to, and chloride above the normal level, but bicarbonate was still extremely low. Dehydration had been partly overcome: both serum proteins and hemogloblin indicated that the

blood was less concentrated; and the blood non-protein nitrogen had begun to fall. The condition of the patient, meanwhile, had improved greatly. During the next three days administration of sodium chloride, glucose and water was continued vigorously, and in addition larger amounts of bicarbonate were given. At the end of this period the non-protein nitrogen had fallen almost 100 mg. per cent, the serum electrolyte picture was practically normal, respirations were quiet, consciousness was restored, and the patient was able to sit up and take food and fluids by mouth with relish. The points to which I wish to draw chief attention are: first, the simultaneous depletion of base, bicarbonate and chloride; second, the improvement that followed partial restoration of body fluids, and base, even when chloride was driven above and bicarbonate remained far below the normal concentrations; third, the necessity for administration of bicarbonate to meet the specific deficiency of this element in a subject who, because of impaired renal function, was unable, by exercising the usual selective activities of the kidneys, to make proper adjustments between ions.

Examples of this kind, involving a great variety of conditions not usually classified as diseases or disorders of metabolism, could be multiplied indefinitely to emphasize the value of chloride and bicarbonate determinations in the analysis, and in the treatment of patients with dehydration. However, these must suffice because I should like to touch on one other subject before closing.

With increasing knowledge of the chemical processes of bone formation and the effects of hormones and vitamins, analysis of blood has come to serve a useful purpose in the diagnosis of diseases of bone and disorders of calcification. There are one or two points to which I should like to call attention in this connection. First of all, the calcium of serum is not an independent variable. A certain fraction, which is apparently inactive, is combined with the serum proteins. Within certain limits, therefore, the concentration of calcium in serum varies with that of

protein. These variations seem to have no influence upon either calcification or muscular irritability. In order to interpret serum calcium in relation to these functions, protein should be determined at the same time. Secondly, bone is not composed of calcium alone, but also of phosphate and carbonate, particularly phosphate, and there is a tendency for calcium and inorganic phosphate of serum to vary inversely. For this reason phosphate should also be measured with calcium. Many erroneous impressions may be avoided if it is made part of routine procedure always to determine protein and inorganic phosphate of serum with calcium.

In every respect, but especially in relation to calcium and phosphate, the blood must be considered merely as a transportation medium. It serves to carry calcium and phosphorus from the gut, whence they are absorbed, to their great storehouse in the bones, or from the bones to the gut or kidneys by which they are excreted. From the concentrations of these elements in the blood serum alone, one can gain but an imperfect impression of calcium metabolism. Calcium in serum may rise either because it is being absorbed from the gut with unusual rapidity or because the bones are giving up excessive amounts. Low serum calcium may be referable to diminished absorption from the gut, increased deposition in the bones or accelerated excretion in the urine. The levels of phosphate and protein as determinants of serum calcium have already been mentioned. These and other factors that influence calcium solubility may be regarded as affecting the capacity of the transportation system. The causes of any disturbance of serum calcium and phosphate levels must be analyzed with consideration of all these variants, before a diagnosis can be made and therapy intelligently directed.

In Table 2 have been listed some of the most frequent causes of such abnormalities and the disturbances of function by which they are produced. It is quite evident that diagnosis from chemical examination of the serum alone must be highly unsatisfactory. It can be greatly

Table 2. The effects of various common physiological disturbances or diseases on calcium and phosphorus metabolism. 0 = no effect, — = diminished, + = increased. No distinction has been drawn between calcium and phosphate in relation to absorption, excretion and bone formation.

Condition	Absorption	Excretion	Bone Formation	Serum Ca	Serum P	Serum Protein
Vitamin D deficiencies	—	0	—	.	.	.
Rickets (in infants)—Osteomalacia (in adults)				0		
Usual picture in active stages				—	—	0
During repair or when diet is low in calcium or high in phosphorus				—	0 +	0
Fatty diarrhea. Probably improper absorption of vitamin					0	0
Renal rickets. In some cases faulty absorption of calcium, benefited by vitamin D				—	+	—
Vitamin D excess Associated with metastatic calcification	+	0 +	—	+	0 —	0
Parathyroid excess	0	+	—	+	0 —	0
Parathyroid deficiency	0	—	+	—	0 +	0
Thyroid excess	0	+	—	0	0	0
Thyroid deficiency	0	—	+	0	0	0
Acidosis or acidifying measures	+	—	—	+ —	+ 0	0
Renal rickets (osteoporosis) due to nephritic acidosis				—	+ 0	0 —
Conditions with low serum proteins	0	0	0		0	
Nephrotic syndrome	—	—	—	—	+	—
Malnutrition (protein starvation)	?	?	?	—	0	—
Osteitis deformans (Paget's disease). The serum picture and metabolic abnormality depend on stage and severity of the disease	0	+ —	+ —	+ —	+ —	0
Bone tumors—Serum picture depends on rapidity of bone destruction	0	+	—	0 +	0 +	0
Myelomatosis	0	+	—	0 +	0	0 +

facilitated by measurements of calcium and phosphorus intakes and outputs, but these require time and facilities that are rarely available. In most instances, however, a diagnosis can be established with the aid of x-rays of the skeleton and other types of clinical examination. This can, perhaps, be illustrated by description of a few cases.

A woman, 22 years old, was first seen in 1924, when she entered the hospital complaining of pains in her knees and hips and frequency of urination. Examination revealed fractures of the neck of both femora, patchy rarefaction of all bones, involving especially the pelvis, a urine loaded with pus from which streptococcus viridans was repeatedly secured in pure culture, a phenolsulfonphthalein excretion varying from 20 to 35 per cent and blood non-protein nitrogen slightly elevated. A diagnosis of osteomalacia was made. Although this long word has a satisfying sound, it is nothing more than a descriptive term. The important matter was to determine the cause of the softening and resorption of bone. The patient, who was followed for some years, entered the hospital repeatedly, usually because of fractures or some other symptoms arising from the disorder of calcification. During these years renal function continued to deteriorate under the influence of the infection, but she had few symptoms referable to the kidneys. The decalcification became gradually greater and more generalized. The results of chemical examinations of the serum are shown in Figure 4. The solid line, representing non-protein nitrogen gives a rough indication of the steady deterioration of renal function. Serum calcium is always reduced to a variable degree; phosphate lies at the upper limits of normal at first, rising somewhat as the disease progresses. Throughout the period of observation serum chloride was extremely high, while bicarbonate was proportionally reduced. A hyperchloremia (or chloride acidosis) of this kind is the typical effect of the administration of acidifying chloride salts such as ammonium chloride. As the administration of such salts leads to decalcification of the bones, it seems reasonable

to refer the osteomalacia in this patient, not to the usual deficiency of vitamin D, but to this endogenous chloride acidosis, which was probably connected with her renal insufficiency. Determinations of calcium and phosphorus alone, in this case, could have contributed but little, even if they had not proved positively misleading. There is evidence to indicate that acidosis is the immediate cause of many cases of so-called "renal rickets."

July 18, 1930 a white male, 60 years old, was sent to the hospital with a diagnosis of hyperparathyroidism. For three

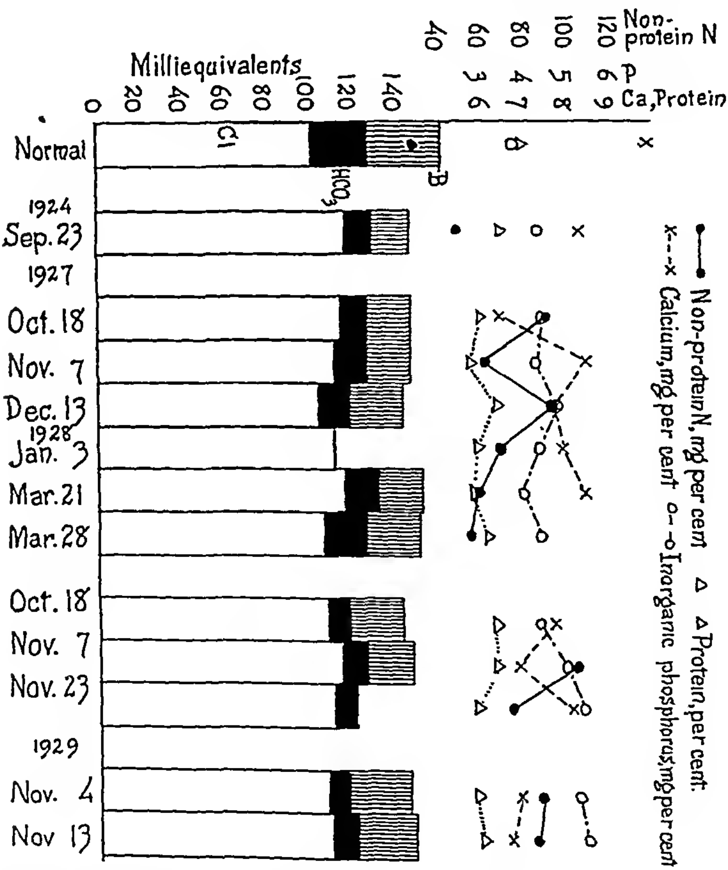

Fig. 4. Chemical changes in the serum of a patient with chronic renal disease and generalized osteoporosis.

years he had suffered from weakness, indigestion, anorexia and loss of weight, and increasing pains in his trunk and limbs. Extreme decalcification of the bones with some deformities, and a profound anemia with a high color index were discovered in November, 1929. The latter did not respond to oral treatment with liver and iron. Because of the weakness, general decalcification of the bones and high calcium in the serum, a diagnosis of hyperparathyroidism had been made. On admission he was desperately weak and emaciated. There was general decalcification of the bones with collapse of some vertebrae, and striking anemia with a high color index. He remained in the hospital until his death on Feb. 3, 1931. Both anemia and bone disorder defied all treatment and before his death he sustained many pathologic fractures. The calcium of the serum was very high, 12 to 18 mg. per cent, the inorganic phosphorus variable, 1.8 to 5.5 mg. per cent. With this picture in the serum and demonstrated negative balances of calcium and phosphorus, a diagnosis of hyperparathyroidism was warranted, according to the criteria proposed by Barr, especially since no Bence-Jones protein could be demonstrated in the urine. His serum proteins, however, proved to be extremely high, 9.8 to 13.0 per cent, in spite of a low albumin, 2.2 to 3.2 per cent. The serum protein was predominantly composed of globulin, which varied from 7.1 to 10.6 per cent. Because of this hyperglobulinemia and the anemia a diagnosis of general myelomatosis was made. At autopsy this diagnosis was confirmed and the absence of any parathyroid tumor or hyperplasia was also established. It has been claimed that decalcification of the bones with high serum calcium and normal or low inorganic phosphate is pathognomonic evidence of hyperparathyroidism. This is only one of many cases that prove the fallacy of this claim. Hypercalcemia has been reported by others and seen by us in patients with metastases of carcinoma in the bones. It is not unlikely that it indicates nothing more than the presence of a process causing exceedingly rapid destruction of bone. It can, therefore, be interpreted only with due consideration of x-ray findings

in the bones and all other significant clinical data which can be secured by other methods.

It may be relevant, in this connection, to mention that we have recently seen a case of hyperparathyroidism with no disturbance of calcium, phosphorus or protein in the serum. The diagnosis was established by the presence of diffuse decalcification of the bones with some tumors of the osteitis fibrosa cystica type and bilateral renal calculi.

The significance of abnormal concentrations of lipoids in the serum is still so obscure that the discovery of such abnormalities is of more interest than clinical value. Association of high serum fat and cholesterol with the nephrotic syndrome and certain types or phases of diabetes has long been recognized; but cannot be interpreted in terms that are useful for diagnostic or therapeutic purposes. There is good reason to believe, however, that as knowledge of lipoid metabolism advances, determination of serum fats, phospholipids and cholesterol will have to be added to the diagnostic armamentarium.

Part of the confusion of this chapter of blood chemistry may be due to general failure to recognize that lipoids, like proteins, are unable to traverse capillary membranes. For this reason, as Dr. Evelyn Man has recently demonstrated in our department, changes of blood water are reflected in proportional alterations in the concentrations of blood lipoids.

It may seem extraordinary that blood sugar has received no consideration. This omission implies no lack of appreciation of the importance of blood sugar measurements; it is prompted only by the fact that the subject has received so much more attention than other chapters of blood chemistry, that it has seemed best to devote the limited time at my disposal to the aspects of blood chemistry which have been less generally emphasized.

In conclusion I can only reiterate the opinions I expressed earlier: that it is unfortunate in the extreme to limit the application of chemical analysis of the blood to any selected group of technical procedures or to any one class of diseases, or to treat the information secured by these analyses as if it were separable or distinct from other types of clinical information.

CLINICAL OBSERVATIONS AND LABORATORY INVESTIGATIONS ON THE 1933 EPIDEMIC OF ENCEPHALITIS IN ST. LOUIS*

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Encephalitis, as it appeared in the epidemic in St. Louis in the summer of 1933, was an acute febrile disease, characterized by prominent signs of meningeal irritation, a comparatively short course, and a relatively low incidence of sequelae.

Early in the epidemic, hospitalization was strongly recommended by the Health Division, with the result that over 90 per cent of the reported cases were observed in hospitals. In the Isolation Hospital, where nearly 400 cases were treated, a senior student, responsible for the completeness of the records, was placed by Dr. Barr. The present report covers 300 of these cases, and free use has been made of the tabulations prepared by Mr. Robert L. Drury, a member of the senior class at Washington University.

Classification. The cases have been divided into three groups by Dr. T. C. Hempelmann[1]. The first two groups differ in the mode of onset, and the third group consists of abortive or very mild attacks in which the diagnosis was difficult and frequently uncertain.

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* Department of Internal Medicine, Washington University, School of Medicine, St. Louis.

Read before the Annual Meeting of the Academy, January 4, 1934.

Onset and Initial Symptoms. The first type of onset was abrupt, and preceded by no prodromal symptoms. Headache and fever appeared, frequently associated with vomiting. Very rapidly the patients became somnolent, spoke slowly and with some difficulty, and at times went to sleep without finishing a sentence. A stupor from which the patient could be aroused to answer simple questions frequently followed closely on the appearance of somnolence, and in some cases true coma occurred. Mental confusion was commonly present. Instead of somnolence and stupor, many patients showed irritative phenomena, such as restlessness, constant irrational talking, or, rarely, active delirium.

The second type of onset was characterized by a prodromal period, usually lasting one to four days, in which slight fever and "grippy" feelings were usually present. At the termination of this period a sharp rise in temperature occurred, and the subsequent picture was similar to the first type.

The predominant features of the disease were meningeal

TABLE I.

TYPES OF ONSET

*Sudden	57.0%
Gradual	42.3%
Doubtful	0.6%

or meningo-encephalitic. Some degree of rigidity of the neck muscles was present in 86 per cent of the cases, and a positive Kernig's sign in 72 per cent. The abdominal reflexes were ordinarily absent, and the deep reflexes were diminished or absent. Plantar reflexes were abnormal in 40 per cent of the cases, but this was variable, and the findings would sometimes change from hour to hour. Tremors of the tongue and lips were frequent, and were especially noticeable when the patient attempted to speak.

* Any onset of less than three days duration was arbitrarily classified as sudden for purposes of tabulation.

Symptoms or signs referable to the eyes were comparatively rare, and usually consisted of small and sluggish pupils, blurred vision, or photophobia. Nystagmus and diplopia each occurred in 8 per cent, and strabismus and ptosis in 3 per cent and 2.6 per cent respectively. The accuracy of these last two figures is still open to some

TABLE II.

NEUROLOGICAL SIGNS

Abnormal deep reflexes	74.0%
Absent abdominal reflexes	59.6%
Tremors	55.6%
Abnormal plantar reflexes	40.6%
Aphasia or speech difficulty	12.0%
Facial weakness	6.0%

question, since it has not been possible to determine the condition of all of these patients prior to their attack of encephalitis, and since ptosis was more a weakness and slight drooping of the lids than an actual paralysis.

Mild and Abortive Cases. In some cases a slight fever of one or two days duration, with perhaps some stiffness of the neck or headache, prompted lumbar puncture, which revealed the increase in cells characteristic of encephalitis. At times an unexplained fever was the only symptom. In children the findings were more variable and mild cases seemed to be more common.

Spinal fluid. Lumbar puncture usually yielded a clear fluid under moderately increased pressure. In the majority of instances from 100 to 300 cells were present per c. mm., but this was subject to considerable variation, and one count as high as 1100 cells per c. mm. was recorded. Lymphocytes predominated, but in a few instances polynuclear cells constituted from 30 per cent to 50 per cent of the total count. At times the fluid withdrawn on the first puncture was normal, while a second puncture a day or two later showed the characteristic increase in cells. When the results of spinal punctures are tabulated, it is seen that 81 per cent showed 10 or more cells per c. mm. If, how-

ever, as is probably more correct, counts of 3 or more cells per c. mm. are considered abnormal[2], only 7 per cent of the cases showed normal cell counts.

A slight increase in globulin was demonstrated in 41 per cent by means of the Pandy test.

Sugar determinations usually showed from 50 to 90 mg. per cent, and very rarely was the result low enough to lead to a suspicion of tuberculous meningitis. Spinal fluid was precipitated as soon as collected, and the filtrate was used in determining sugar by the Shaffer-Hartmann method.

Blood. Blood counts most frequently showed white cells ranging from 10,000 to 14,000, with extremes of 2,800 and 36,000. With the Schilling differential, the usual result was a shift to the left.

Clinical Course. The clinical course was rather characteristic. Fever continued high, quite commonly between 104 and 105° F., for a few days, and then gradually diminished, in the majority of instances reaching normal in six to ten days after admission to the hospital. Frequently there was a critical drop in temperature, which then usually remained normal in uncomplicated cases. A few times the elevation of temperature was more prolonged, and in fatal cases the temperature usually remained elevated up to the time of death. Somnolence and stupor, when present, usually persisted until about the time of defervescence, and then rapidly disappeared, as did the other symptoms and physical signs. The rapidity of recovery in many instances was amazing, and at times a patient who at one visit could only be aroused with difficulty, would on the next day be alert and apparently perfectly normal.

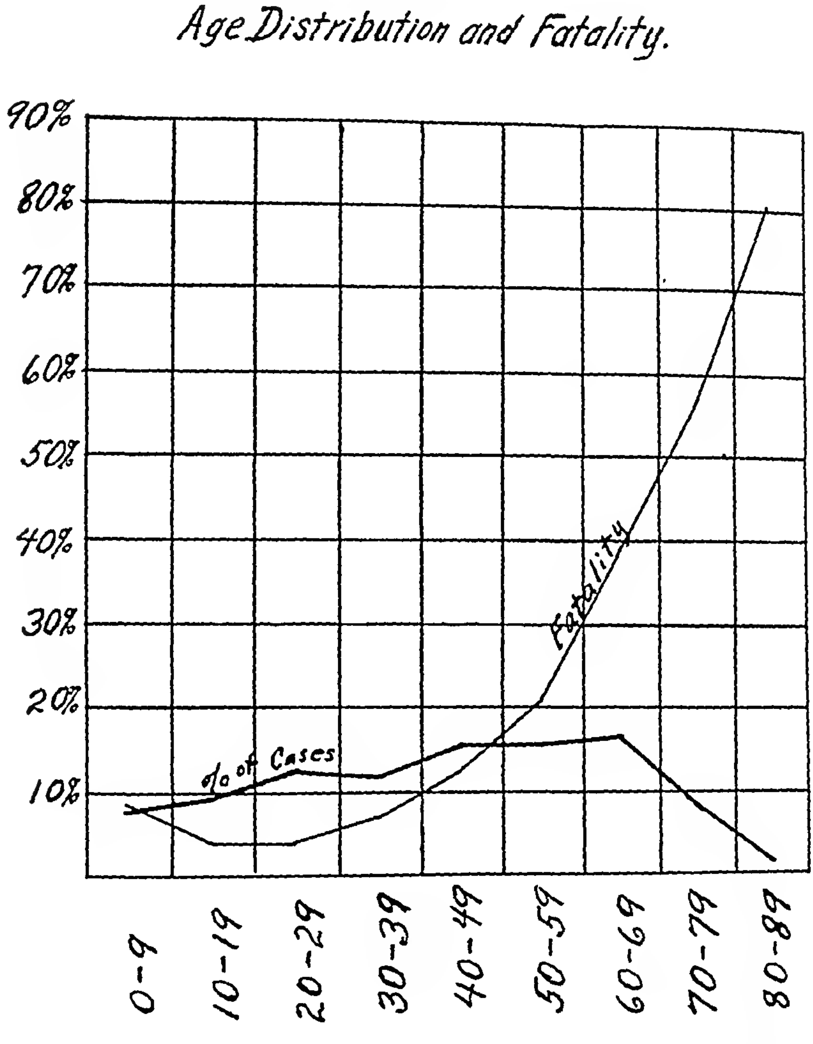
TABLE III.

*DEFERVESCENCE (200 CASES)

By lysis	55.8%
By crisis	44.2%

* For purposes of tabulation a return of temperature to normal in 36 hours or less was considered critical; more than this was considered defervescence by lysis.

*CHART I.



Complications. Most of the deaths were associated with some other condition. Of the 68 deaths occurring in this group, 42 were complicated by bronchopneumonia. Nephritis, hypertension, and arteriosclerosis were also frequent concomitant conditions, and were probably present before the appearance of encephalitis. Of the deaths occurring

* These curves are prepared from the data on 1091 cases of encephalitis reported to the St. Louis Health Division.

in the Isolation Hospital only about 10 per cent were without some complication diagnosed clinically.

Prognosis. The prognosis was much more favorable in younger individuals, as is shown by the fact that while 41.3 per cent of the cases reported in the epidemic were under 40 years of age, only 11.4 per cent of the deaths occurred in this group (Reports on 1091 cases to the St. Louis Health Division). The rise in the death rate with advancing age is graphically demonstrated when the curves of incidence and fatality are plotted on the same chart (Chart I).

Condition on Discharge. The condition of most patients on discharge from the hospital was surprisingly good except for some general weakness. Only 4.6 per cent showed any residua, and half of these consisted of such difficultly definable conditions as were recorded as mental or emotional abnormality. Only a detailed observation over a long period by the psychiatrists will make an evaluation of such findings possible. Photophobia was still present at discharge in two patients. Parkinson's syndrome appeared only one time. Lumbar puncture at the time of discharge, after three weeks isolation, showed a pleocytosis still present in several instances, although such examinations were not made routinely. No relapses or second attacks have been observed in this group of cases.

Treatment. Treatment was symptomatic. The most commonly employed measures were lumbar puncture for increasing headache or other evidence of advancing disease, and the intravenous administration of hypertonic glucose. A number of other therapeutic agents were employed, but none on a large enough scale for the results to be of significance.

Differential Diagnosis. Some cases of non-paralytic poliomyelitis probably cannot be differentiated with certainty from encephalitis. Poliomyelitis was present in St. Louis during the past summer, but the number of cases was not unusually large, so that mistakes in all probability were very few.

Tuberculous meningitis presented much more difficulty, but the onset is ordinarily more insidious, the spinal fluid sugar is usually markedly lowered, and the demonstration of tubercle bacilli would eliminate any doubt.

Follow-up. Plans have been made to follow the recovered cases for a period of two years. An examination of some of the patients 3 months after recovery has not shown any significant deviation from their condition at the time of discharge from the hospital.

Identity of the Disease. The relation of this illness to the lethargic encephalitis of v. Economo[3] naturally comes into question. The sudden, stormy onset, the acute and relatively short course, the predominance of signs of meningeal involvement, the low incidence of cranial nerve paralyses, and the rarity of residua seem to justify placing it in a separate clinical group. It is realized that cases indistinguishable from these have occurred in previous epidemics, but they were only a small fraction of the total number of cases. The clinical manifestations that we have observed, and the seasonal occurrence, correspond quite closely to encephalitis occurring in Japan[4] which has been classified as Type B.

Pathological changes occurring in the two types are quite similar, and consist of perivascular infiltration and some nerve cell destruction. Differentiation is probably more difficult for the pathologist than for the clinician.

Nevertheless, the clinical uniformity of such a large group of cases, which differ from most cases of lethargic encephalitis (v. Economo) requires that the possibility of different etiological agents be kept in mind.

Experimental

Early in the epidemic, research was centralized in the laboratories of the Departments of Medicine and Pathology of Washington University. This enabled experimental study of all cases in which collection of material would not interfere with work planned by the institution in which the patient was treated. Dr. Charles Armstrong, of the

National Institute of Health collaborated in this investigation throughout the course of the epidemic[5].

Many cultures of blood and spinal fluid were made with uniformly negative results, and animals of a number of species were inoculated with blood, spinal fluid, and filtered nasal washings from acute cases, and with brain tissue removed aseptically at autopsy. Shortly after beginning this work, some of the rhesus monkeys developed symptoms suggestive of encephalitis, and work with other animals at the time was to a large extent discontinued.

Emulsified brain tissue from fifteen cases was inoculated intracerebrally into rhesus monkeys, and in seven instances these animals developed fever, weakness, tremors and incoordination after an incubation period of from 8 to 21 days. These symptoms varied in degree, and sometimes were quite mild. The majority of animals showing symptoms were sacrificed, and passage in series through 5 monkeys was successful with four strains. Histological examination of the central nervous system showed changes consistent with human encephalitis, namely, perivascular cuffing and nerve cell degeneration. No bacteria were demonstrable.

Passage in monkeys was attended with considerable difficulty. Only about 40 per cent were susceptible, a large inoculum was necessary, and reinoculations were usually made after an interval of five days. At the time that this phase of the work was discontinued at Washington University and transferred to Dr. Armstrong at the National Institute of Health, one strain was still active in monkeys in our laboratory.

Among other animals, six horses and mules were used. One mule developed fever, lasting a few days, about ten days after inoculation but showed no other evidence of illness. Another mule, inoculated with monkey brain, developed fever and became obviously ill after about ten days. This animal was sacrificed, and histological examination of the brain revealed perivascular cuffing. Passage in this species was not successful, so the significance of the observation is open to question.

During the course of this work, glycerinated brain tissue was shipped to a number of laboratories. Dr. Webster[6], of the Rockefeller Institute, used a strain of mice, bred in his laboratory, which is highly susceptible to neurotropic viruses. In four out of eight attempts he was able to isolate a virus causing encephalitis in these mice. This virus was neutralized by sera from convalescents and was not neutralized by sera collected from normal individuals in New York.

Dr. Webster informed us of his findings, and we accordingly inoculated stock mice with brain tissue of monkeys showing signs of encephalitis. On first inoculation the takes were irregular, but on passage the virus became capable of causing the death of nearly 100 per cent of the animals. Three of the strains that were being passed in monkeys were established in mice. We have confirmed Dr. Webster's observation that the virus is neutralized by the serum of individuals convalescent from attacks of encephalitis during this epidemic.

This virus differs from that of herpes in a number of its characteristics, and at this point it should be stated that over thirty rabbits and eight cebus monkeys were inoculated with brain, blood, spinal fluid, or nasal washings without once encountering herpes virus. These results make it seem evident that herpes virus did not play a part in the St. Louis epidemic.

After intracerebral inoculation, the incubation period that we have observed in mice ordinarily varies between four and eight days, and is most commonly five or six days. At the expiration of this period the mice become hyperirritable and many have convulsive seizures. In a few hours they become quiescent, respiration is barely perceptible, and they will move only when strongly stimulated. Death follows shortly, and histological examination of the brain reveals perivascular cuffing and nerve cell degeneration.

The virus deteriorates fairly rapidly on standing, as is shown by the following experiment. An emulsion of fresh brain was diluted serially and inoculated immediately.

All of the mice given a dilution of 1-1,000,000 died. After standing for five hours at room temperature, only the dilutions up to 1-1,000 caused the death of all inoculated animals; and after 24 hours at room temperature this occurred only with the 1-10 dilution.

TABLE IV.

DETERIORATION OF VIRUS ON STANDING

	Immediate Inoculation	After 5 hours room temperature	After 24 hours room temperature
1-10	*3/3	3/3	3/3
1-100	3/3	3/3	2/3
1-1,000	3/3	3/3	1/3
1-10,000	3/3	1/3	
1-100,000	3/3		
1-1,000,000	3/3		

* These fractions indicate the number of mice dying over the number inoculated.

There is a gradual deterioration in 50 per cent glycerine in the ice box, but after 5 weeks we have demonstrated active virus, although only a few of the inoculated animals have succumbed, and the incubation period was prolonged.

The frequency with which this virus has been encountered, and its neutralization by the serum of patients convalescent from encephalitis lead one to think that it was of etiological significance in the St. Louis epidemic.

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THE THOMAS W. SALMON MEMORIAL COMMITTEE REPORT AND PRESENTATION OF PORTRAIT OF THE LATE DR. THOMAS W. SALMON*

Mr. President, Fellows and Members of the Academy:

I appreciate the honor of having been requested by your President to appear upon the program of this Annual Meeting. In behalf of the Thomas W. Salmon Memorial Committee of the Academy, I wish briefly to account for our stewardship.

In keeping with the obligations assumed by this Committee, as agent for the Academy, the fields of psychiatry and mental hygiene have been surveyed in this country and abroad and the names of twenty-seven leaders in psychiatry, neurology, mental hygiene, psychology and the social sciences have been before the Committee for more than a year as possible recipients of the Salmon Lectureship award. The recent and remote contributions of these scientists have been made a matter of record and in the archives of the Committee future accomplishments will be recorded.

It is a great pleasure to be able to advise the fellows of the Academy of the unanimous selection of Dr. C. Macfie Campbell, as the Thomas W. Salmon Memorial Lecturer for the year 1934. Dr. Campbell, Professor of Psychiatry at Harvard University since 1920, has been an active participant in all the leading movements for the advancement of psychiatry. He was for a number of years President of the Massachusetts Mental Hygiene Society. He delivered the Shattuck Lecture in 1924 on "Psychiatry and the Practice of Medicine," the Gehrmann Lectures in Hygiene at the University of Illinois, in 1932, on "The Schizophrenia Problem"; and the Lowell Lectures in Boston, in 1932, on "Human Personality and the Environment." His experience in directing a hospital which deals with a wide variety of social problems associated with psychiatric conditions and his eminence in the psychiatric world are so well known that it is unnecessary to review in detail his many contributions.

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* Read at the Annual Meeting of the Council of The New York Academy of Medicine, January 4, 1934.

The Salmon Memorial Lectures will be given here on April 13, 20 and 27, 1934.

Not only has the Committee been charged with the responsibility of selecting the Salmon lecturer, but upon it has devolved the task of stimulating advance in psychiatry and associated fields within the resources at its command. To this end eighteen applications for financial assistance of research projects have been reviewed by the Committee. The large number of applications for aid necessitated the formulation of a policy which favors subsidizing research which can be made effective by a grant of a comparatively modest amount.

The following projects were chosen for subsidies by the Committee:

Miss Muriel T. Bashlow, Judge Baker Foundation—for studies on "Psychometric results of clinical psychotherapy in cases of emotional blocking among juveniles."

Dr. Clarence O. Cheney, New York Psychiatric Institute—for "Endocrinological studies in psychiatric patients."

Dr. Franklin G. Ebaugh, Colorado Psychopathic Hospital, Denver—for "Studies on treatment of epilepsy with Emmenin (the name applied by Professor Collip of McGill University to a hormone he has isolated from human placentas)."

Dr. Norman Fenton, Bureau of Juvenile Research, California—for "A study of the mental and social traits of four hundred boys in a State correctional school and the relationship of these traits to later behavior on placement."

Dr. John Levy, New York—for "An experimental study of therapeutic approaches to enuresis."

Dr. Jacob Kasanin, Clinical Director, State Hospital for Mental Diseases, Howard, Rhode Island—for the purchase of an oscillometer for "Investigation of the peripheral circulation in schizophrenia."

significance may be of special interest to the physician—for while I am not trained in medicine, I have been especially requested to address myself this evening, in-so-far as I can, to the point of view of the practitioner. At least we can meet on the ground of a common interest in the enhancement of health.

I shall not begin by defining the vitamins. I do not know any good definition for vitamins as a group; and I think I do know some good reasons for not attempting any.

Firstly, and *most fundamentally,* the fact should be fully realized and constantly kept in mind, that it is only as an accidental result of their having been discovered in a more rapid succession than they could be physically isolated and chemically identified that the vitamins ever came to be grouped together and called by a group name. *They are not a natural group.* The more we learn about them the less alike do they appear, whether in chemical nature or in nutritional function.

Each vitamin is entirely specific in the sense that no one or combination of them can take the place of any other one.

While details of molecular constitution are still being worked out, enough is known of at least vitamins A, B, C, and D to show that these four substances belong to four radically different types of organic compounds.

Correspondingly, their functions in the body are radically unlike.

Whenever, then, the physician has reason to think that he may be dealing with a vitamin deficiency—or, if not with a manifest deficiency, then with a condition in which a more liberal vitamin intake would be beneficial—the question *which* vitamin becomes increasingly insistent as the unlikeness of the individual vitamins is rendered constantly clearer by current research.

And the practitioner's utilization of present scientific knowledge of the vitamins can proceed with the greater confidence in view of the fact that none of the postulated

additions to the present list of vitamins represents any strictly new concept such as might overturn our present views—they all represent rather the refinement of present views through subdivisions of existing concepts.

Thus a few years ago the refinement of knowledge of vitamin B led to its subdivision into two parts: a more heat-labile, now called vitamin B or B_1; and a more heat-stable, now called vitamin G or B_2. Each of these two parts is now apparently in process of being again subdivided, the first into B_1 and Reader's B_4[1]; the second by the setting off of what Chick and Copping call the Y factor from the rest of vitamin G or B_2[2]—in each case a differentiation rather than the introduction of any radically new concept.

Secondly, two independent digests of the knowledge available up to about 1932, each representing a concensus of expert opinion, one British[3] and the other American[4], comprehending the clinical as well as the laboratory point of view, have recently made available a sufficiently well-balanced, well-matured body of subject-matter and interpretation, so that in many respects the physician can now feel that he has as well authenticated a basis for his practical judgments in matters respecting the vitamins as in many older fields.

In the British report, which explicitly states that every part of its text represents the study and judgment of all of its authors, it is stated that: "So far as Western civilization is concerned, it is no doubt true that the rareness of the occurrence of frank deficiency diseases, such as scurvy, xerophthalmia and beri-beri, indicates that an absolute deficiency of vitamins scarcely ever exists in the individual diet. On the other hand, it is now becoming generally recognized that much subnormal health and development, and even incidence of disease, are associated with a partial deficiency of one or more of these necessary substances. The influence of such partial deficiencies, even when relatively slight, may be extremely serious when they occur in early life . . . There is also danger that the effects of such

partial or latent deficiency may persist as a chronic condition throughout adult life." . . . And they emphasize the statement that, *"latent deficiency disease* is a real thing and not an imaginary concept."

In the volume issued by the American Medical Association, Mendel writes: "Existing knowledge permits little more than vague speculation respecting the mode of action of vitamin A . . . For the present it may be wiser to stress the indefinite function of the vitamin in preserving 'health and vigor' rather than to herald any specific action against definite microbiotic enemies. Deficiencies of any sort tend to decrease the ability of the body to resist disease." And in another article of the series, Eusterman and Wilbur, writing explicitly from the clinical standpoint say: "Until recently the versatility of vitamin A has apparently not been appreciated." Thus the fact that vitamin A is entirely specific among the vitamins in the sense that no other can take its place, is consistent with the fact that its function in serving the well-being of the body and as an *aid* to the ability to resist infection may be a more "versatile" or more generalized function than that of aiding against a single species of pathogen.

Hess, writing on vitamin C in the same series of articles says: "Another point that has been brought into prominence in connection with adult as well as infantile scurvy is its intimate association with the infectious process . . . one of the most striking and important symptoms of scurvy is a susceptibility to infection (furunculosis, nasal diphtheria, grippe, etc.)."

Thus while each vitamin is a specifically essential substance for which no other known substance can be substituted, yet shortages of certain vitamins may increase the body's susceptibility to more than one species of infection —yet, again, this does not mean to *all* infections equally.

A third general principle to be borne in mind is that, whatever therapeutic properties individual vitamins may possess, *a vitamin is primarily a nutritional factor.*

Thus in the introduction to a recent concise review contributed by the Department of Physiological Chemistry at Yale[6] we read:

"The mass of pertinent experimental evidence at present available forces the conclusion that the conception of the vitamins is not a fad; indeed, it is rapidly ceasing to be looked upon even as a biochemical novelty but is rather accepted as one of the fundamental principles of nutrition."

Perhaps it should be emphasized, even at the risk of repetition—that the practitioner will often realize most satisfaction from thinking of the vitamins as nutrients rather than as drugs.

The British Committee's remark of some years ago upon the blurring of the nutritional significance by "pharmacological bias" still holds food for thought. Any practitioner may at any time be dealing with cases in which no vitamin can supply the specific pharmacodynamic action that is desired, yet in which whatever medication is employed will yield a more satisfactory result if attention is also given to the general nutritional well-being of the body by ensuring a liberal intake of any vitamin of which there may conceivably have been even a relative shortage. Thus, in the clinical article already referred to, Eusterman and Wilbur, after referring to the rarity of xerophthalmia in the United States, add: "It is likely, however, that certain individuals, the poor in particular, do not consume enough foods that contain vitamin A and vitamin G to insure a state of nutrition essential to the greatest physical stamina, efficiency, and ability to resist infectious diseases." And Wilder, in his address as Chairman of the Section on Pharmacology and Therapeutics at the Eighty-second Annual Session of the American Medical Association, referred to "the increasingly probable condition of mild or incipient avitaminosis" and further said: "I am convinced that many cases of dissatisfaction with treatment are accounted for by the partial starvation which results from incompletely balanced diets . . . In many

diseases the possibilities of therapeutic benefit from supplying nutritional elements in amounts greater than those required for maintenance in health is today receiving augmented attention."

Then too, the physician, in addition to employing the newer knowledge of nutrition not to supplant but rather to supplement his accustomed therapeutic methods, has also the opportunity to teach the patient (while *as patient* he or she is in a teachable frame of mind) how to acquire and maintain throughout the rest of life a nutritional condition superior to that which he would otherwise enjoy—or endure. The degree of well-being which is prevalent in the community need by no means be accepted as representing the physician's objective for his patient. No less high and conservative an authority than F. Gowland Hopkins has stated[5] that, "a race or community is found in equilibrium with an environment which includes its food supply. It is often forgotten that such environment is fortuitous and that the equilibrium reached is one in which the community, while managing to survive, may yet be functioning at levels far below those possible to its innate capacities. It is truths of this sort that the science of nutrition, having reached the stage of controlled experiment, is now demonstrating." He also says:

"It is often felt that concerning matters so urgent as our own nutrition, humanity, with all the experience of the ages behind it, can have little to learn from modern science, yet, as in the case of so many other established traditions, an assumption of this kind is wholly unjustified. Tradition accumulates prejudices quite as often as truths, and the former are apt to be more potent in their influence." . . . And:

"That scientific research during recent years has greatly emphasized the importance of right nutrition as a factor in human welfare is very sure . . . We now know that conditions recognized as actual diseases develop because the supply of some minute nutritional necessity has failed, while, short of obvious disease, ill-health may depend upon

a lesser degree of such deficiency . . . In all individuals such a lack may greatly increase the liability to infection by bacteria and other parasites."

So much for the general consideration of the topic assigned me. The following brief statements regarding individual vitamins are all intended to be construed in the light of these general principles: (1) the highly specific nature of each vitamin in the sense that nothing else can take its place; (2) the possibility that a vitamin may nevertheless have a bearing upon the ability of the body to resist more than one species of infection; and (3) the general principle that a vitamin is primarily a nutritional rather than a pharmacological factor—and may, on that account, be all the more important to the physician who takes the long view of the well-being of the patient.

II.

Some Observations with Reference to Individual Vitamins

Vitamin A is a fat-soluble substance conspicuously essential to growth, and also very important to the maintenance of vigorous health at all ages.

In addition to the effect of vitamin A in maintaining, as the Journal of the American Medical Association puts it, the integrity of the body's first line of defence against infection, it also has a further influence. For in the carefully controlled experiments both of Lassen in Copenhagen and of Boynton and Bradford in Rochester, it was found that when infective organisms were introduced by injection so that the battle was staged entirely beyond the 'first line of defence', the ability of the body to resist the infection was again found much higher in the animals which had received the more liberal intakes of vitamin A. This is not necessarily a matter of the immunological mechanism as now understood; but it is a fact which we are probably not justified in ignoring, even if we cannot yet fully understand it.

Time does not permit more than the mention here of the very large amount of laboratory evidence that vitamin A taken in amounts above those which actual necessity requires, yields increasingly beneficial results in higher levels of vitality or standards of positive health.

Hess, Lewis, and Barenberg, in the Journal of the American Medical Association for August 26, 1933 discuss the question, "Does Our Dietary Require Vitamin A Supplement?" I think the answer should depend upon the dietary. Their controlled observations in a model child-caring home have not indicated decrease of respiratory infections as a result of increasing the intake of vitamin A above that which the dietary of the institution regularly afforded.

The 24 ounces of milk mentioned as regularly contained in their daily dietary probably by itself furnished each of these children well over 1500 International units of vitamin A per day; other articles of their liberal dietary enrich it still further in this respect; and these children probably entered the periods of controlled observation with fairly good stores of vitamin A already laid up in their bodies. A large proportion of the children of the United States and of New York City are less fortunate in these respects. May we therefore hope that the careful observations of Hess, Lewis and Barenberg will be interpreted to the credit of the nutritional condition of the children under their care, and not to the discredit of vitamin A?

Their findings constitute strong evidence against the exaggerated impressions which they and some others in this country and Harris and some others in England believe to be more or less prevalent; but perhaps it should be pointed out that where in such researches the evidence is conflicting, that which represents positive findings is usually fully as significant as that which is negative.

There is positive ("field") evidence of wide differences of vitamin A intake even among people of like economic status, depending upon their food habits, and there is also positive (laboratory) evidence that the dietaries richer in vitamin A tend to yield better results in the long run; but to avoid any possible misconception may I emphasize in the same sentence that I am speaking of such enrichment of vitamin A intake as may be had by the wise use of everyday articles of food?

Vitamin B (B_1). This is the substance the study of which as a preventive of beri-beri called general attention to the vitamin concept about 20 to 25 years ago. It was found that the neuritis of beri-beri could be prevented (and if not too far advanced could be cured) by many natural foods, and that from these foods a specific antineuritic substance could be extracted. The existence of this substance was established and the investigation of it was well advanced, before the coining of any such word as vitamin.

The outstanding characteristics of vitamin B are its antineuritic value and its value for the maintenance and promotion of appetite.

Its properties as a growth-essential and as in some way helping to keep the body in good tone and resistant to some types of infection, may be equally important but are less distinctive since some of the other vitamins also serve in such ways as these.

Speculations as to just "how it acts in the body" have perhaps been even more rife around vitamin B than about the other vitamins. Few if any of the other theories rest upon such substantial experimental evidence as does Cowgill's view[4,6], that while "the question of the exact function of this vitamin remains unsolved" there is a quantitative relation between the vitamin B requirement and the total energy metabolism or requirement. This point of view, with a full realization of the important influence

of vitamin B upon the appetite, may often be of therapeutic value. Varying circumstances may well lead to different answers in different cases as to when one should employ a vitamin B concentrate and when enrich the intake of vitamin B by increasing the proportion of the natural or less highly refined articles of food in the diet. The former will, of course, suggest itself in those cases in which a very large or very sudden increase is desired, while the latter has the advantage that it contributes to the enrichment of the intake of other important nutritional factors at the same time.

In the presence of Dr. Hess who has investigated so extensively both vitamins C and D and of Dr. Mendel whom we always wish to hear as often and as fully as opportunity permits, I shall but mention these two vitamins and then close with a few observations regarding vitamin G or B_2.

Vitamin C prevents and cures scurvy; but if we were sure that we should never see a case of scurvy we would still have ample reason to be interested in vitamin C. Hess has described how often children without distinctive scurvy symptoms are yet in need of more vitamin C in order to do their best. Wolbach, Howe and Church have shown the importance of vitamin C to the nutrition of the bones as well as of the soft tissues; and discussion in a recent issue of the Journal of the American Medical Association suggests that more liberal intake of vitamin C may perhaps be helpful in combating arthritis. Dolldorf relates it to capillary condition. Very likely our knowledge of the ways in which vitamin C serves the nutritional welfare of the body is still far from complete; yet already enough is known to suggest strongly that diets rich in vitamin C may be helpful in a wide variety of cases even if not specifically indicated by the symptoms observed.

Vitamin D is perhaps as dramatically effective against rickets as is vitamin C against scurvy. Is it, then, also a nutritional asset in which it is desirable to enrich the diet liberally at all ages? There are others present who can discuss this question better, so I leave it to them.

Vitamin G has so recently been differentiated from vitamin B that on many points much yet remains to be done to assess the relative responsibilities and merits of these two essential substances. It might be premature to assign to vitamin G any such clear-cut pharmacological function as that of vitamin B in the prevention and cure of beri-beri; but the suggested relationships of vitamin G both to pellagra and to pernicious anemia, and its recently demonstrated relation to the development of cataract all seem to call for careful consideration of the possibility that diets rich in vitamins A, C, and G may be helpful in a number of connections. We know that vitamin G has far-reaching effects on the well-being of our experimental animals.

Supplementing the summaries already mentioned ([3,4,6]) reference may also be made to the still more recent summary paper of Day[7].

As Day points out, Goldberger and Lillie[8] were the first to describe the pathological condition in the rat due to a deficiency of what is now termed vitamin B_2 or G. Other laboratories soon confirmed and extended their general findings[9,10,11,12,13].

Goldberger and associates produced also an experimental condition known as black-tongue in dogs, and from similarities of symptoms (and their observations to the effect that all could be prevented or cured by the feeding of the same materials) they were led to suggest[14] that pellagra in man, black-tongue in dogs, and the condition chiefly characterized by dermatitis in rats are all due to the same nutritional deficiency. In commenting upon this theory Underhill wrote[4]: "The discovery of the potency of the unknown factor termed vitamin G is an undoubted advance in the knowledge of pellagra, but it is clearly unwise to assume that vitamin G deficiency and pellagra are necessarily synonymous terms."

The caution thus suggested by Underhill would seem to be doubly justified, on the one hand by the developments in

the study of pellagra, and on the other by the fact that vitamin G deficiency is now known to give rise to other important effects in addition to the pellagra-like dermatitis.

Particularly important are the eye conditions described by Day and his coworkers[7,15] and independently confirmed by O'Brien[16] and by Yudkin[17].

Thus vitamin G deficiency may be both less and more than clinical pellagra. Here as elsewhere, the attempt to assign the vitamin a physiologically or pharmacologically descriptive name is apt to throw undue emphasis upon what (however important in itself) is only one feature of its nutritional significance.

The work of Ellis in the writer's laboratory[18] is affording strong evidence that a higher level of intake of vitamin G may distinctly influence the degree of nutritional well-being and resulting health and vitality, even though the lower intake is already above that at which any characteristic sign of nutritional deficiency appears.

We therefore believe that vitamin G not only prevents deficiency disease but has positive functions in normal nutrition as well, and that optimal nutrition requires a much more liberal intake of vitamin G than simply that which is demonstrably necessary for the prevention of any characteristic sign of deficiency.

In the foregoing discussion the term vitamin B or B_1 is allowed to stand for the whole of the more heat-labile, and the term vitamin B_2 or G for the whole of the more heat-stable, part of the vitamin B complex. The writer has no doubt that each of these two primary divisions of the vitamin-B complex is a multiple rather than a simple nutritional factor; but the necessity for brevity forbids the attempt to analyze the evidence in this paper. The nutritional considerations here briefly summarized will lose nothing of their significance when it becomes possible to assign them, or if necessary to reassign them, as properties of more precisely defined chemical substances.

As I began by saying that we have no definition of the vitamins, I may end by saying that we do not know how many vitamins there are. We have, however, good ground for believing that our present concepts cover the essentials and that further discoveries will be differentiations within the lines already well conceived; and will therefore not upset or supplant our present knowledge of the vitamins but rather supplement and refine it.

There is much knowledge now at hand which seems certainly sound so far as it goes; and I believe that it goes far enough to be capable of rendering good service to medicine, not only in remote contingencies but also in everyday practice.

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THE EFFECTS OF MODERATE DEFICIENCY OF VITAMINS*

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The physician in his practice has learned to recognize and to treat successfully the diseases due to the outspoken deficiency of vitamins. Those of us who live in the North know rickets; those in the Orient know beriberi; those in the South know pellagra; a few of the fortunate have seen xerophthalmia; and all are familiar with scurvy. We are told, however, that much ill-health is due to a moderate deficiency of vitamins; that the food of modern mankind, in the process of manufacture, selection and preparation, has lost some of its virtue. The laboratory worker, with his colonies of animals, discovers some half dozen new deficiencies a year; and suggests that symptoms in man, similar to those of his animals, are due to similar deficiencies. The manufacturer, given a little time, is able to furnish a preparation containing the indicated vitamin —succeeds in having clinical trials made, and finally so advertises the product to physician and often to layman, that the physician does not dare to neglect prescribing it for vague symptoms which puzzle him. Considerable money changes hands—some not infrequently finding its way into the research laboratory which holds the patent. But I would like to remind you that the real evaluation of each and every one of these remedies rests with the clinician. The physician Eijkman, in Java, noted that pigeons fed for economical reasons on boiled polished rice from the hospital kitchens, developed polyneuritis, resembling that of patients with beriberi. The Danish pediatrician, Bloch, showed that xerophthalmia and night blindness could be cured by cod liver oil, but not by sunlight; also that these conditions occurred independently of rickets;

* Delivered, November 1, 1933.

pregnancy may be in large part responsible for this mortality is accumulating. Toverud, working is Oslo, has found that the Norwegian diet especially in winter, results in a negative balance of calcium and of phosphorus; that this can easily be prevented by the use of more milk, green vegetables, fruit, and cod liver oil. The birth-weight of full-term infants was thereby increased; and the percentage of premature births among unmarried mothers dropped from 32 per cent (in the obstetrical clinic) to 2 per cent among the mothers cared for by Toverud. At the Maternity Center of New York by careful supervision of hygiene during pregnancy, the incidence of premature births has been reduced to 1/3 of that prevailing in the general population of the City. Several factors of course play a role in the decrease of the rate of premature birth. The dietary deficiency undoubtedly includes that of calcium, phosphorus and vitamin D.

The typical disease due to lack of vitamin D is rickets. Other factors may play an etiologic role—such as the diet of the mother during pregnancy; low birth weight; and rapid growth. The effect ascribed by E. Mellanby to cereals in the production of rickets may in part be due to rapid growth or to the low assimilation of the phosphorus in cereal. The phosphorus of cereals is present chiefly as inositol hexaphosphate; which is not only poorly absorbed but which also precipitates calcium, and thus prevents its absorption. In certain cases of rickets, the typical symptoms and signs, although present, may not be so prominent as signs usually regarded as minor: for example, extreme irritability. We have observed several cases in which the irritability disappeared within a few days, while the serum phosphate rose in response to ultraviolet radiation. In another case, sweating was profuse; the hands were red and swollen, and the skin of the fingers was macerated and infected—suggesting acrodynia. However, the blood pressure was normal and signs of rickets were obvious; the abnormal condition of the hands rapidly disappeared under antirachitic treatment. Such cases may have given rise to the idea that ultraviolet therapy is bene-

ficial in acrodynia. We have not found it so. Another condition allied to rickets, but with none of the skeletal changes is the tetany occurring in children of low birth weight within the first six weeks of life. Such cases usually respond in a dramatic manner to intensive antirachitic therapy. Dental caries in older children has been ascribed by M. Mellanby to dietary deficiency, particularly to a relative deficiency of vitamin D and to a diet high in cereals. Boyd and his coworkers report that dental caries may be arrested by a diet containing pigmented vegetables, fresh fruit, butter, milk and cod liver oil. Hanke and his coworkers believe that the addition of one pint of orange juice and the juice of one lemon to the ordinary diet will check the development of caries. Disagreement prevails among competent workers in regard to the relative effect of diet and of acid-producing microorganisms in causing caries. More carefully controlled clinical studies are now in progress in several places; and we should soon know more definitely which are the important factors.

Definite indications exist that a relative deficiency of vitamin C may exist in certain parts of the world, even where scurvy is rare. Göthlin and his colleagues have refined a test for capillary fragility—first proposed by Dr. Hess; by aid of this, it has been possible to show in two adults that the capillaries of the skin become more fragile after a diet low in vitamin C had been taken for several weeks; and returned to normal within a few weeks after a diet high in vitamin C had been resumed. A rather extensive survey among school children in northern Sweden revealed the presence of a considerable number in whom the capillary fragility was increased. A good correlation existed between this and the low antiscorbutic value of their diets. Gingivitis appeared more frequently in the children with increased fragility, but was present also in the others. Gerstenberger has used fresh fruit in large quantities in the treatment of aphthous and ulcerative stomatitis, apparently with success. Hanke and his coworkers have made extensive studies in which one pint per day of orange juice

appears to have greatly decreased the incidence and severity of gingivitis in a community of children at Mooseheart. They imply that the effect is due to vitamin C. It must, however, be pointed out that owing to its carotene content, orange juice may have a vitamin A activity greater than that of milk. It also contains an appreciable amount of calcium. The anemia in scurvy may yield to orange juice. Rohmer and Bindschedeler describe prescorbutic anemia in infancy—accompanied by poor growth in weight and stature, irritability, anorexia, and puffiness of the face, feet and hands. In several of their cases, cure of the anemia could not be accomplished with a dried cabbage juice rich in vitamin C, until iron also was added.

Deficiency of the vitamin B complex has long been suspected in the dietary of infants, largely on the basis of assays using experimental animals. Maurer, reasoning on rather a priori grounds, believes that neonatal death is due to insufficient vitamin B in the diet of the mothers during pregnancy. The importance of this subject would justify a most extensive study. Hoobler, Bloxsom, Dennett and others have described a symptom-complex in children 6-12 months of age, which they ascribe to relative deficiency of vitamin B. The symptoms are anorexia, pallor, loss of weight or stationary weight, irritability, and muscular rigidity. The symptoms yield to the use of yeast, yeast extracts, and preparations of wheat germ. The effect, however, may be due in large measure to a greater intake of food. From our own experience, we can say that many cases with similar symptoms do not respond to this treatment. We have felt that the chief etiological factors in our cases were faulty methods of feeding, or the presence of infection. In the latter type, we have often observed immediate and lasting improvement following the use of 1 or 2 units of insulin twice a day continued for a week or ten days. Vitamin B may be relatively deficient in the diet of older children. In an admirably planned clinical experiment, Summerfeldt of Toronto, shows that the expected average gain in weight in a group of children can be

increased four times over a period of three weeks by the use of a special cereal, in place of ordinary cereal. These gains were maintained. It is difficult to know whether such gains are really optimal; whether they may reasonably be attributed to vitamin B is also open to some question, because the cereal furnished also considerable additional minerals, including calcium, phosphorus and iron. Patients with chronic diarrhea may be given diets low in vitamins; they may also absorb vitamins poorly. It seems likely that the smoothness of the tongue noted in some of these conditions may be caused by partial lack of vitamin B_2; for it is relieved by giving brewer's yeast.

Vitamin A has been the subject of recent clinical study by Dr. Hess and his colleagues. There can be no doubt from their investigations that the administration of large quantities of vitamin A in the form of haliver oil, or provitamin in the form of carotene, did not confer the slightest additional power upon infants to resist respiratory infections. This is to be attributed to the fact that these children were already receiving a diet rich in vitamin A. According to Sutliff and Segool, cod liver oil will not prevent otitis media as a complication of scarlet fever. We have found that carotene is also ineffective (Figure 1). On the other hand, it seems possible from a study of the carotinoid content of the blood, which we have carried out, that about 15 per cent of children over the age of two years, may avoid foods rich in carotene, and as a consequence about 1/3 of them may be subject to repeated respiratory infection. We feel also that a diet rich in vitamin A may be desirable in the first few months of life. It is known that infants—especially of low birth weight—may have in their tissues a comparatively very low store of this vitamin. Although they may not at this time be subject to infection, owing to the presence of protective substances acquired from the mother, they may later on show increased susceptibility, unless they receive more vitamin A than is present in milk alone. We have carefully studied two groups of infants in the out-patient department.

The Effect of Oral Administration of Carotene During Scarlet Fever

Cases Uncomplicated at Onset			Cases Complicated at Onset			
No Carotene 21 Cases	Carotene 13 Cases		No Carotene —13 Cases—		Carotene —16 Cases—	
		Complications	Initial	After 1 wk.	Initial	After 1 wk.
1	0	Otitis	8	1	8	8
2 (same case)	0	Mastoiditis	0	5	1	13
1	2	Adenitis	2	4	3	2
0	1	Arthritis	0	1	0	0
0	0	Sinusitis	2	0	3	1
0	0	Abscess	1	0	2	3
0	0	Empyema	1	0	0	0
0	0	Peritonitis	0	2	0	0
2	3	Other	0	2	0	2
0	0	Died	—	1	—	1
4.3	5.2	Av. Stay, Wks.	6.9		6.1	

Fig. 1.

Infections of Infants as Affected by Diet

From Barenberg and Lewis, New York City and Maxwell, Rochester, N. Y.

	New York City		Rochester, N. Y.	
	C. L. O.	Viosterol	Good	Bad
J. F. M.	0.35	0.25	0.24	0.50
A. M. J.	.23	.18	.15	.22
J. A. S.	.19	.15	.08	.14
O. N. D.	.33	.17	.23	.32

Fig. 2.

Eighty of these received cod liver oil at least from the age of two months; most of them from the age of two weeks; and until at least the age of six months. From this time, they received pigmented vegetables. The rate of infection (number of infections per infant per month) is nearly the same as that in the series of Barenberg and Lewis (Figure 2). The other group of 40 infants received no cod liver oil; until after the age of four months. Many of them received vegetables from the age of six months. The milder

respiratory infections—rhinitis, pharyngitis, otitis media —occurred with equal frequency in both groups, excepting in the early Spring months (Figure 3). In the various

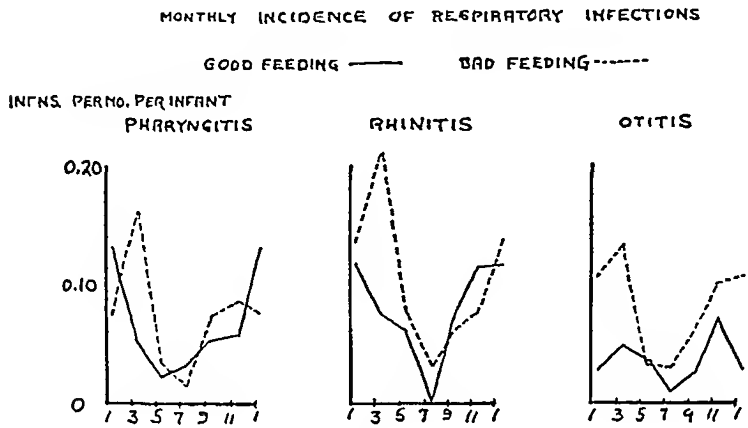

Fig. 3.

age groups, there is little difference in the incidence of rhinitis and pharyngitis, but a marked increase in the incidence of otitis media in the poorly-fed group after the age of six months (Figure 4). We feel that our groups are too small to permit very certain conclusions, and we would emphasize the difficulty in excluding other causes than

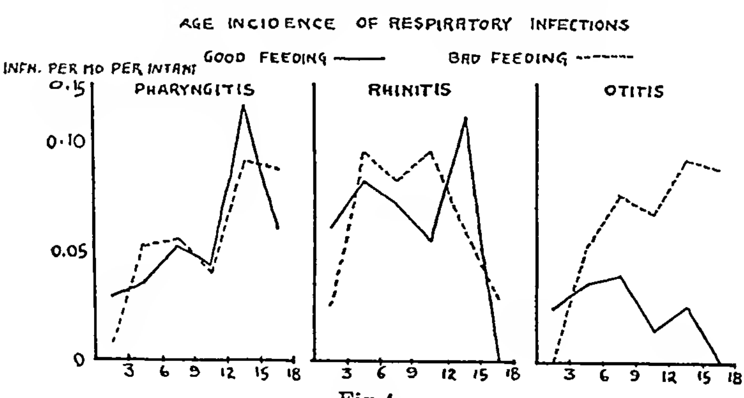

Fig. 4.

faulty diet. In another study, we have some evidence that early feeding of cod liver oil may prevent the occurrence for severe infections, such as pneumonia, mastoiditis, and septicemia (Figure 5). Here we are dealing with only a

Correlation of Infections with Previous Feeding

DIET			0-6 Mos. INFECTIONS, %				6-24 Mos. INFECTIONS, %				
C. L. O.	Veg.	Number	O	Mod.	Sev.	Sev./Total	Number	O	Mod.	Sev.	Sev/Total
0	0	35	40	37	23	0.38	50	14	40	16	0.54
+	0	27	56	29	15	0.34	21	9.5	86	4.5	0.05
0	+						77	25	60	15	0.21
+	+						56	41.1	55.4	3.5	0.06

DIET			2-6 Yrs. INFECTIONS, %				6-14 Yrs. INFECTIONS, %				
C. L. O.	Veg.	Number	O	Mod.	Sev.	Sev./Total	Number	O	Mod.	Sev.	Sev/Total
0	+	267	32.5	55.1	12.4	0.18	712	55.9	39.6	4.48	0.10
+	+	124	60.5	34.7	4.8	0.12	123	62.6	32.5	4.88	0.13

Fig. 5.

single observation in each case, and relying upon the history as well as we could obtain it. In another study we have analysed the records of about 700 children who entered the hospital before the age of three years. We have considered separately the sexes; have indicated the ratio of severe to non-severe infections; and have attempted to correlate the influence of (a) bad diet as causing severity of infection; and (b) exposure to children of school age in the family as causing severity of infection. These two latter correlations are based upon Yule's method of coefficients of contingency. A coefficient of plus one is regarded as a perfect correlation; plus 0.5 as very good; zero, as absence of relation. Good diet is defined as before—cod liver oil from the age of two months to at least six months; either cod liver oil or vegetables from the age of six months. The age-incidence (Figure 6) of relatively severe

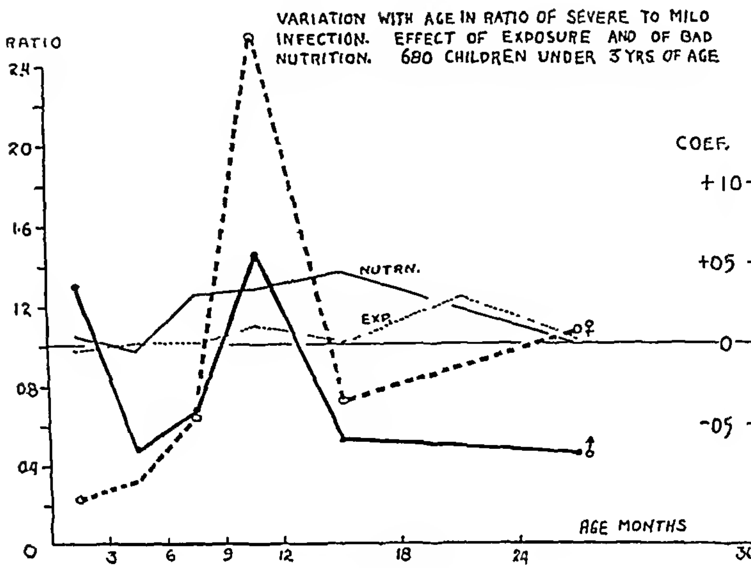
VARIATION WITH AGE IN RATIO OF SEVERE TO MILD INFECTION. EFFECT OF EXPOSURE AND OF BAD NUTRITION. 680 CHILDREN UNDER 3 YRS OF AGE
RATIO
2.4
2.0
1.6
1.2
0.8
0.4
0
COEF.
+10
+05
0
-05
NUTRN.
EXP.
AGE MONTHS
3
6
9
12
18
24
36

Fig. 6.

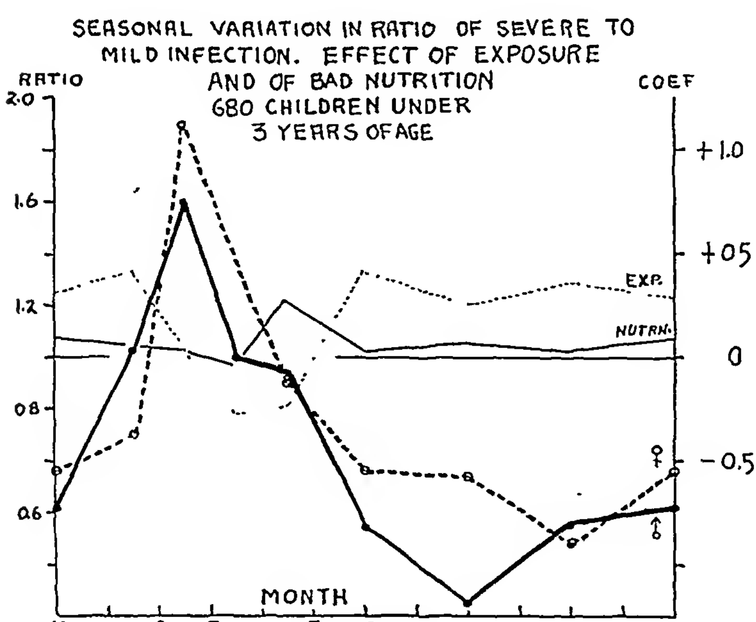
SEASONAL VARIATION IN RATIO OF SEVERE TO MILD INFECTION. EFFECT OF EXPOSURE AND OF BAD NUTRITION
680 CHILDREN UNDER 3 YEARS OF AGE
RATIO
2.0
1.6
1.2
0.8
0.6
COEF
+1.0
+05
0
-0.5
EXP.
NUTRN.
MONTH
12
1
2
3
4
5
6
7
8
9
10
11
12

Fig. 7.

infection indicates that boys are relatively much more liable than girls under the age of three months. Thereafter, girls are more liable. This is regarded as an effect of constitution. Exposure to older children—and incidentally—greater economic distress—cannot account for the high incidence in both sexes of relatively severe infection between the ages of nine and twelve months. On the other hand, there is some evidence that the relative severity of infection may be associated with poor diet consumed in the earlier months of life. In the seasonal incidence of severe infections (Figure 7), we observe that the sexes are affected nearly alike; the girls suffering somewhat more at all times. Infants who have a severe infection during the summer months are likely to have had previously a poor diet. The very marked increase in severity of infection in February is not related to exposure, and only to a slight degree related to faulty diet in the earlier months. We may regard this high peak of severe infections as due either to more massive exposure, or to increased virulence of the infection. These studies are not offered with a view of settling the question of the relationship of vitamin A to infection; but rather, in order to keep the question open. They indicate, moreover, that the factors involved in infection are many, including constitution (sex, even during infancy), exposure, the nature of the infection, and probably also diet. I would stress in particular that if vitamin A has any anti-infective power, it should be administered in the earliest months when the growing organism may need larger quantities, and when a deficiency is more likely to exist.

NON-DIABETIC KETOSIS IN CHILDREN*

OSCAR M. SCHLOSS

When katabolism of fat is normal, it is completely burned to carbon dioxide and water and only traces of ketone substances which arise as intermediary products of its oxidation can be detected in the body fluids or in the urine and expired air. The survival of ketone substances due to incomplete fat katabolism leads to their accumulation and excretion in abnormal amounts and gives rise to the metabolic perversion termed ketosis.

It occurs in its severest form as a complication of diabetes and the illuminating investigations in connection with this disease have contributed largely to our knowledge of its mechanism. The occurrence of ketosis of serious magnitude is not, however, confined to diabetic persons. In the young especially, non-diabetic ketosis is not infrequent and may threaten life and require energetic treatment for its alleviation.

It has long been known that young persons affected by various disorders are prone to excrete ketone substances in their urine; but after puberty this tendency is minimized. In adult life, non-diabetic ketonuria of pronounced grade is rarely observed except in starvation and even then, is of much lesser magnitude than is observed in children.

The tendency to ketosis in the young is not confined to the human as shown by Allen's experiments on dogs. A diet high in fat led to very severe ketosis when fed to puppies, but was practically without effect on grown dogs. The tendency of the young to ketosis is obviously an expression of some metabolic peculiarity.

It is my purpose to discuss the non-diabetic type of ketosis as it affects children with special reference to its clinical manifestations; also with such consideration of its etiology and mechanism as our present knowledge of the subject permits.

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* Delivered November 2, 1933.

Subsequent to the demonstration by Hirshfield in 1895 that ketosis results from insufficient metabolism of glucose, much has been done to elucidate this action. The observations of Knoop, Magnus-Levy, Schwartz, Embden, and others show that the oxidation of the straight chain fatty acids with an even number of carbon atoms leads to the occurrence of aceto-acetic acid which is oxidized only as a result of the simultaneous combustion of glucose indicating the occurrence of a reaction in which glucose and aceto-acetic acid are involved. The nature of this reaction and all of the forces participating are still undetermined despite many pertinent investigations. Shaffer, however, has shown by in vitro experiments, that in an alkaline medium and in the presence of peroxides, aceto-acetic acid is destroyed by glucose. If aceto-acetic acid is not destroyed, it accumulates in the body fluids being changed in part to beta-hydroxybutyric acid by reduction and to acetone by decomposition. All three substances are excreted in the urine and acetone also in the expired air. Further advances contributed by Zeller, Lusk, Ladd and Palmer, Shaffer, Woodyatt and others have served to clarify the quantitative relationship involved in the ketolytic action of glucose. With certain exceptions, to be mentioned later, it seems that the complete oxidation of aceto-acetic acid requires the simultaneous combustion of definite proportions of glucose. According to this conception, Woodyatt and Shaffer have appraised the ketogenic and anti-ketogenic components of foods metabolized expressing this relationship by means of ratios.

Calculated according to the method of Woodyatt, when the metabolized fatty-acid-glucose ratio exceeds 1.5 in adults, acetone substances appear in the urine. This corresponds to a ketogenic: anti-ketogenic ratio of 1 when computed on a molecular basis by the method of Shaffer. Such ratios must necessarily apply only to material actually metabolized for, aside from the possibility of food escaping absorption, it has been shown by Richardson and Ladd and others that when the diet is high in fat, excess fat may be stored and energy derived from the consumption

of body glycogen. The ratios cited apply only at the threshold of ketosis, for as larger amounts of fat in relation to glucose are metabolized, the actual amount of ketone substances eliminated are much less than these ratios would lead one to expect. Under these conditions, Shaffer found that it was necessary to assume a molecular ratio of 2, twice the threshold value, in order to obtain an agreement between calculated ketone formation and actual excretion. Assuming that the present conception of the destruction of aceto-acetic acid is correct, it appears that the ketolytic action of glucose is somewhat variable. There are, indeed, observations which suggest that there may be modifying influences on this reaction, and it is certain that appraised on the basis of present knowledge, the destruction of aceto-acetic acid in the course of fat katabolism does not constantly and necessarily conform to a strictly molecular reaction with glucose. A very good example of this inconsistency is the smaller ketolytic action of glucose in children than in adults.

The readiness with which children excrete acetone substances in their urine has naturally incited curiosity and investigation. The most illuminating observation in this connection was made by Wilson, Levine and Rivkin. When children metabolize a mixture with a fatty acid to glucose ratio of .7, acetone appears in the urine thus disclosing that at the threshold of ketosis children require twice as much glucose to metabolize completely a given amount of fatty acid as adults. It seems therefore unnecessary to assume that children store or mobilize glycogen less efficiently than adults. Indeed, all experimental evidence is to the contrary. The fact that during fasting the blood sugar declines more rapidly and to a lower level in children than in adults observed by Shaw and Moriarty, Weymuller and Schloss, and others, is easily explained by the greater demand on stored glycogen. It appears therefore that when energy is being supplied largely by the combustion of fat, due usually to restricted carbohydrate ingestion, children need more glycogen than adults thus justifying the assumption that the deficiency in glycogen storage is relative and not absolute.

Accessory influences which favor the ready development of ketosis in children are the normally high metabolic rate which is increased by fever and the diminished carbohydrate intake during fever due to loss of appetite or vomiting. We do not know on what the normally low fatty acid to glucose ratio of children depends, but there is probably, as Allen suggests, some specific biologic factor. This may perhaps be related to the accelerated endocrine growth stimulus during this period. Hints as to the possible influence of the pituitary can be gleaned from the experiments of Anselmino and Hoffman, Houssay and Burns and Ling, but such implications are at present too speculative to merit more than passing notice here.

The mild degree of ketosis so readily developed by all children during the course of acute infections or conditions accompanied by some degree of carbohydrate starvation has, as a rule, no clinical significance, since as far as can be determined, in its milder forms it is not responsible for characteristic symptoms. It seems that these milder forms of ketosis are so controlled that the organism is able to defend itself against harmful effects. In contrast to the usual benign form, there are certain peculiarly susceptible children who develop a degree of non-diabetic ketosis which may prove as severe and threatening as diabetic coma. There is no simple laboratory test or physical characteristic which differentiates children with this susceptibility. They are so designated only by the observation that severe ketosis is provoked by conditions with only trivial effect on other children. The familiar clinical manifestations of ketosis vary in severity from slight drowsiness to severe coma or convulsions. The symptoms are largely referable to the central nervous system and in the milder forms drowsiness or somnolence may be the only objective sign which in most cases disappears even without treatment. Occasionally, however, beginning with slight drowsiness the sensorium becomes progressively duller until the deeply comatose child with flushed face, red lips, air hunger, tissue dehydration, acetone breath, and severe pros-

tration presents a picture which on superficial examination cannot be differentiated from that of diabetic coma. Serious symptoms such as these are not always of gradual onset but may supervene suddenly within the course of a few hours. It seems probable that the tendency to develop severe ketosis is an expression of a constitutional peculiarity of the individual, a magnification perhaps of the susceptibility of children in general, but at any rate, a metabolic fault which renders him liable to severe ketosis provoked by conditions which are without effect on the ordinary person. The existence of this susceptibility is recognized by most observers and is exemplified by observations of Weymuller and myself that when fed diets high in fat, susceptible children develop a grade of ketosis much greater than normal children.

The cause of this peculiar reaction has been the subject of much speculation but its nature still remains obscure. We can, of course, be sure that the fundamental difficulty lies in a disproportion between the relative amounts of glucose and fat metabolized, for even if there were no experimental or chemical evidence for this view the striking effect of glucose administered to children suffering from severe ketosis would be ample proof. But it is when we attempt to elucidate the manner in which metabolism is thus disturbed that difficulty is encountered. In the presence of pronounced ketosis, the blood sugar falls very rapidly and this was considered by Hilliger, Ross and Josephs, Rumpf and others to demonstrate deficient storage of glycogen. Wilson, Levine, and Rivkin, Weymuller, I, and others have observed, however, that under the influence of high fat diets or fasting, the blood sugar of normal children is reduced as much as that of children especially predisposed to ketosis. Moreover, the same observers found no indication that susceptible children stored glycogen less well than normals. Therefore, despite the simplicity and attractiveness of this theory, one must conclude that it is unsupported by sufficient evidence.

Another possibility to be mentioned is that susceptible children may require more glucose for the complete metabolism of fat than normal children, just as normal children use glucose less economically than adults. Unfortunately, there is insufficient evidence to appraise this possibility. To do this, it would be necessary to determine the amounts of glucose and fat actually metabolized by means of the respiratory quotient. So far as I am aware this has been done only once. In a child susceptible to severe ketosis provoked by cyclic vomiting Wilson, Levine, and Rivkin found that the ketogenic-antiketogenic ratio at the threshold of ketosis did not differ from that of normal children. The hypothesis has also been advanced that there may be some inherent difference between children in their tendency to burn fat. The normal child always burns glucose in preference to fat. If the diet is high in fat, excess fat is stored and the composition of the metabolic mixture stabilized by the consumption of stored glycogen. Wilson, Levine, and Rivkin observed that this tendency to restrict the combustion of ingested fat was lacking in a child susceptible to severe ketosis. Weymuller and I noted that when fed identical high fat diets susceptible children developed a much greater degree of ketosis than normal children. We ventured to suggest the possibility that susceptible children have a greater tendency to burn fat than normal and are thus deprived of a useful protective mechanism. Much more evidence is necessary to establish the validity of this hypothesis, but at present it seems of sufficient importance to merit passing mention. On purely speculative grounds one could suggest other perversions of metabolism which might conceivably predispose to severe ketosis, but a consideration of these would offer little illumination of a subject concerning which experimental data is the prime necessity, and for this reason I shall proceed to more practical aspects of the subject about which, fortunately, more is known.

In the clinical laboratory, ketosis is usually recognized by the presence of a positive nitro-prusside test in the urine.

This is a very delicate test and the reaction is striking in the presence of even very small amounts of acetone. As an uncoordinated observation, it designates in no way that ketosis is of clinical importance. Due to disregard of this knowledge, symptoms may be attributed to ketosis which are actually dependent upon another cause, often an obscure infection. A similar misconception is the prevalent belief, chiefly among the laity, that acidosis, a term used erroneously as a synonym for ketosis, is a frequent cause of recurring digestive or febrile disorders. The symptoms of ketosis are clouding of the sensorium, ranging from drowsiness to deep coma, rarely convulsions, prostration, air hunger, dehydration, occasionally vomiting, and so far as we know, this is all.

Ketosis may impair the acid-base balance of the organism leading to acidosis but this does not necessarily occur. The effect of small degrees of ketosis may be so fully compensated that there is no impairment of the functional efficiency of the acid-base balance of the body fluids. Involved in this protective mechanism is the formation of the organic base ammonia leading to the conservation of fixed base, the elimination of carbon dioxide by the lungs, and the excretion of acid in the urine. When the degree of ketosis is too great to be compensated, the acid-base pattern of the blood becomes distorted by the utilization of base to neutralize ketone acids. The magnitude of this distortion is in direct proportion to the quantity of ketone acids present at that time. In addition, however, ketone acids are excreted in part at least in combination with fixed base and if ketosis is severe or prolonged, the total fixed base of the body may become depleted. The loss of fixed base as shown by Gamble and his collaborators leads also to loss of water and dehydration may thereby be induced. The presence and degree of acidosis can be best measured in the clinical laboratory by determination of the carbon dioxide content or capacity and the reaction of the blood or serum. For clinical use, knowledge of the carbon dioxide content or capacity of the blood, although not infallible, is usually sufficient.

Thus far I have emphasized the tendency of the ketone acids to cause acidosis but strict accuracy demands brief mention of the exceptional association of ketosis with alkalosis. Haldane and his collaborators observed that the alkalosis of overbreathing or anoxemia may be accompanied by the excretion of ketone substances in the urine. Of more practical importance is the influence of loss of hydrochloric acid by vomiting. If a chlorine deficit be thus induced the blood bicarbonate may be increased even in the presence of considerable ketone acid. Alkalosis of this origin is disclosed by analysis of the blood for chlorine and bicarbonate.

Since the emphasis by Stadelman and subsequent observers of acidosis as the cause of the symptoms of diabetic coma, it has generally been assumed that the symptoms of ketosis are of this origin. The usual association of acidosis with severe ketosis and the observation that acidosis induced in experimental animals by injection of mineral acids causes symptoms quite comparable to those observed in human ketosis suggests strongly that acidosis plays an important part in the causation of symptoms. Moreover, in the non-diabetic ketosis of children there is usually a close correlation between the degree of ketonemia, the presence and degree of acidosis, and the presence and degree of symptoms.

Despite this evidence, the possibility that symptoms may be due to direct toxic action of the ketone substances must be considered. It is known that the administration of acetone to experimental animals may cause profound coma. Hurtley and Trevan found that neutral derivatives of acetone and aceto-acetic acid caused in animals symptoms not unlike those of diabetic coma even including pronounced air hunger. Owing to the neutrality of the substances used in their experiments, they assumed that acidosis was not produced, but they record no data which show that it was not present. All of the evidence bearing on this problem is indirect and is based on the toxic action of ketone substances when given to animals. Until more

evidence is available, the possibility that the ketone substances may cause symptoms directly through their toxic properties must be considered.

Probably the simplest and most easily understood cause of ketosis is the restricted carbohydrate intake of starvation. Under such circumstances, available stores of glycogen are quickly consumed, fat is burned to supply energy and the aceto-acetic acid arising from its combustion finds insufficient glucose to complete its destruction. Except when used for therapeutic purposes, starvation in children results from refusal of food or vomiting. Rarely, however, and then only in the extremely susceptible child does the ketosis of simple starvation cause serious symptoms. Ketosis usually is pronounced after 24 to 48 hours, but despite continued starvation it gradually becomes less intense and may disappear entirely. The blood sugar of fasting children falls very quickly but begins to increase within a few days and may reach normal figures. The alleviation of ketosis by starvation is probably due in part to lowering of metabolism, the restricted consumption of fat, and the utilization of glucose from tissue protein. Whether as an additional protective mechanism, fat is converted into glucose is at present a question too uncertain and controversial to discuss here.

If starvation accompanies a febrile infection, a greater degree of ketosis usually occurs. The accelerated metabolism of fever leads to early depletion of glycogen stores and increased fat consumption. Under these conditions, many of the severe cases of ketosis occur. The type of infection apparently plays no specific role for the same child may develop severe ketosis with successive infections of different types. Scarlet fever, pneumonia, tonsillitis, measles, and other infections may act similarly on the susceptible child.

Starvation preceding and following surgical operations, especially in the presence of a febrile post-operative reaction, is a frequent cause of severe ketosis but with the possible added influence of the anesthetic, so far as has

been determined, involves no other mechanism than has been discussed.

It is probably in relation to so-called recurrent or cyclic vomiting that non-diabetic ketosis in children has aroused most interest. The term has been used to describe a syndrome in children characterized solely by repeated episodes of incessant vomiting always provoked by ingestion of food and water, often spontaneous, lasting in severe cases for as long as a week. After a period of progressive weakness and emaciation, vomiting ceases and recovery ensues. Fatalities rarely occur. The nature of so-called recurrent vomiting is obscure and it is probable that there are different precipitating causes. One child may have an attack at the onset of any acute infection and another may have typical episodes without apparent cause. Sedgwick and Taylor called attention to the importance of chronic infections of the tonsil, a relationship proved by the effect of tonsillectomy in a group of cases sufficiently large to be convincing. This is in accord with my own experience.

Bad posture and visceroptosis were thought by Talbot and Brown and others to predispose to recurrent vomiting.

In many cases, the affected children are of a neurotic type with a neuropathic background and the attacks may be precipitated by any emotional crisis. It therefore seems unlikely that the ultimate cause of so-called recurrent vomiting is single and constant.

With the discovery by Marfan that the urine of such patients contains acetone and perhaps diacetic acid, the belief that ketosis is of etiological importance has become prevalent, indeed to such degree that the term acetonemic vomiting is often used as a synonym especially in the French and German literature.

It is evident that starvation resulting from such severe vomiting will cause ketosis, the degree of which will vary in different individuals and in children especially susceptible, ketosis may be of such magnitude to cause symptoms. This is entirely in accord with all of our conceptions

but ketosis as the primary event directly responsible for the vomiting is an entirely different conception which requires some analysis. Vomiting is a recognized but inconstant symptom of ketosis. Although it may occur during the ketosis of starvation or high fat diets, it does not occur with regularity and when it does occur it is not as persistent or as severe as in recurrent vomiting. Indeed, vomiting may be entirely absent even when ketosis is as severe as that which may accompany an attack of recurrent vomiting. With the exception of a few experiments, attacks of typical recurrent vomiting have not been induced by the ketosis of starvation or high fat diets even in children known to be susceptible to such attacks. The theory that ketosis is the primary event rests largely on the observations of Marfan, Edsall and a few others that acetone may be detected in the urine before the onset of vomiting but it must be pointed out that such observations are few and that frequently acetone is absent from the urine even after vomiting has commenced.

It seems impossible, therefore, that ketosis is of constant etiological importance in so-called recurrent vomiting. That there may be a small group of cases in which such relationship exists is of course possible, but even this assumption would require further and more convincing evidence. It is quite in accord with present knowledge that recurrent vomiting is usually accompanied by ketosis which may be severe but is to be regarded merely in the same light as ketosis which occurs under other conditions.

Obviously, the most important therapeutic measure for the treatment of ketosis, regardless of its cause, is the administration of glucose. When retained it can be given by mouth, if not, it may be given by rectum or by subcutaneous, intraperitoneal or intravenous injection. Glucose even in isotonic solution causes some degree of peritoneal irritation and is absorbed slowly from subcutaneous tissue; therefore, when its need is at all urgent, intravenous injection is the most desirable method of administration. Either a 6 or 10 per cent solution may be used dissolved in freshly distilled water or half normal saline. If the 10

per cent solution is used, 20 c.c. per kilogram of body weight is adequate for the first injection and this is repeated in 3 to 6 hours depending on the symptoms. The injection of this amount should require at least one hour, preferably two, in order to avoid diuresis and resulting dehydration. The intensity of treatment must be gaged by the degree to which the symptoms are relieved. Of chief value for this purpose are hyperpnea, the degree of drowsiness, the intensity of the acetone odor of the breath, and of most value, the carbon dioxide content of the blood. The acetone in the expired air may be estimated roughly by the degree of turbidity produced in the Scott-Wilson reagent. Of least value is the qualitative test for acetone in the urine. Small changes in the excretion of ketone substances are not thus disclosed and acetone may be present in the urine for some time after acute symptoms have disappeared. A rapid decrease of the intensity of the nitro-prusside test, however, is a valuable indication that ketosis is subsiding. The ferric chloride test for aceto-acetic acid is much less sensitive and for this reason gives information of more value.

Before the nature and mechanism of ketosis were understood the resulting acidosis was emphasized and was treated by the administration of large amounts of alkali. This practice is no longer current but to some degree the idea that sodium bicarbonate must be given still persists. For this reason, the rationale of its use is worth considering. When glucose is given in adequate amounts the ketone substances are destroyed and disappear from the blood. The base bound by the ketone acids is thus liberated and the normal acid-base pattern of the blood is restored. It is certain that alkali is unnecessary to neutralize the ketone acids in the blood. Ketosis can be cured quickly and completely without the use of bicarbonate.

In long continued or very severe ketosis, however, the excretion of the ketone acids may deplete the body to some degree of fixed base and to compensate for this loss small amounts of sodium bicarbonate, Darrow's solution or the sodium lactate solution of Hartmann and Senn may be

given, but it is well to emphasize that this treatment is accessory and not essential.

Associated with the loss of fixed base, there is loss of body water with resulting dehydration which, if extensive, may require treatment. If sufficient water cannot be ingested and if the amount given with glucose is inadequate, salt solution must be given by subcutaneous injection. The administration of sodium chloride in this fashion has the additional advantage of replenishing the electrolytes of body fluids.

Some have recommended the use of insulin in addition to glucose with the idea that the glucose would thereby be rendered more effective. Certainly in the ordinary case of ketosis, the use of insulin is not indicated on theoretical grounds for there is no evidence of pancreatic insufficiency. The blood sugar is below normal and the urine does not contain sugar.* It is possible, however, that it may accelerate the combustion and thereby the ketolytic action of glucose and in this way induce more speedy recovery, but the existence of this action and its efficacy as a therapeutic measure can only be demonstrated by further experience.

In this necessarily brief account, I have touched upon current opinion concerning the mechanism of ketosis and have dwelt somewhat upon the non-diabetic form as it affects children. It is unnecessary for me to recount the many deficiencies in our present knowledge of ketosis, both from the viewpoint of physiology and of the clinic. Unfortunately, perhaps, I have emphasized them too freely. In the course of time, however, many of these deficiencies will be supplied and it seems best, in the meanwhile, to reckon consciously with their existence rather than to attempt to fill the gaps insecurely and temporarily with unwarranted speculation.

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* Very rarely one encounters severe ketosis in non-diabetic children accompanied by high blood sugar and glycosuria. The subsequent history of the patient reveals no diabetic tendency. The exact nature of such ketosis is unknown but it seems possible that it is dependent upon temporary pancreatic disturbance. At any rate, it would seem that insulin is clearly indicated in the treatment of cases of this type.

CHARLES DARWIN (1758-1778) AND THE HISTORY OF THE EARLY USE OF DIGITALIS*

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I. *Introduction.*

Before me lie two books, one a great classic in the history of medicine, the other a little known graduating dissertation of an Edinburgh medical student. William Withering's *An account of the foxglove and some of its medical uses* was published in Birmingham in 1785. It is a document that would satisfy the medical humanist, as well as the most rigorous scientific thinker, for its prose compares favorably with the best of the 18th century; and its clinical descriptions of the action of digitalis are clear, shrewd and incisive. His deductions, moreover, are based upon a painstaking analysis of evidence, all in the highest tradition of modern scientific medicine.

The medical thesis, on the other hand, which is entitled *Experiments establishing a criterion between mucaginous and purulent matter. And an account of the retrograde motions of the absorbent vessels of animal bodies in some diseases*, was published in the town of Lichfield in 1780, five years before Withering's book, and two years after its lamented author had died of a dissection wound. In this thesis one also finds an excellent description of the therapeutic action of foxglove. The author of this remarkable booklet bore the name of Charles Darwin, and one is astonished to discover that he died in the year 1778, before having attained the twentieth year of his age. The name of Charles Darwin is sufficient in itself to arouse curiosity, and for some five years I have been attempting to collect

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* An abstract of a paper read January 10, 1934, at the meeting of the Section of Historical and Cultural Medicine, New York Academy of Medicine. The full text with illustrations, contemporary letters and bibliography will be published separately as a brief monograph.

information concerning his career, and concerning the early history of the use of digitalis. My paper, however, which has resulted from this enquiry, will have more to do with Darwin than with digitalis.

The hereditary transmission of mental traits and capacities is nowhere more strikingly illustrated than by the Darwins, who for five successive generations have produced men of outstanding attainments. I need, therefore, scarcely apologize for describing the career of an early and little known member of this remarkable family. Charles Darwin of this memoir died at the age of 19 years and 7 months, a youth of precocious achievements, full of promise and intellectual vigor. His abilities were of a most unusual character; indeed he made so great an impression upon men of his time that, even after 150 years, it has not been difficult to trace from contemporary sources many details of his brief career.

II. *Early Education.*

Charles Darwin was the eldest son of Erasmus Darwin (1731-1802), physician, naturalist, and poet, by his first wife, Mary Howard, the daughter of Charles Howard, a merchant of Lichfield in Shropshire. Charles was born September 3, 1758, in Lichfield when his mother was but 18 years of age. A second son, Erasmus Jr., was born in 1759 and died tragically, probably by his own hand, in 1799 at the age of 40. Erasmus Jr. was given to writing poetry and he had become a successful, though rather eccentric, solicitor in Lichfield some years before his death. Two other children of Mary Howard by Erasmus Darwin died in infancy and the third son, Robert Waring Darwin, who was born in 1766, became a Fellow of the Royal Society at the age of 22 for a paper on ocular spectra (*Philosophical Transactions,* 1788, vol. 76), and was the father of Charles Robert Darwin, naturalist and author of the *Origin of species.* Mary Howard, the mother of these three able boys, became the victim of an obscure disease, probably nephritis incident to child-bearing, and died in 1770, thirteen years after her marriage, when she was scarcely 30 years of age.

Many have commented on the striking fact that Erasmus Darwin transmitted his characteristic qualities of mind to his descendants, and from a close study of Erasmus, the father, and of his son Charles, it seems to me that these peculiar qualities were perhaps more strikingly present in Charles than in the other children. The available data is not complete, but what exists is highly significant. In the short memoir of Charles written by his father as an appendix to his thesis, it is stated that from his infancy he was "accustomed to examine all natural objects with more attention than is usual: first by his senses simply; then by tools, which were his playthings—By this early use of his hands, he gained accurate ideas of many of the qualities of bodies; and was thence afterwards enabled to acquire the knowledge of mechanics with ease and with accuracy; and the invention and improvement of machines was one of the first efforts of his ingenuity, and one of the first sources of his amusement.

"He had frequent opportunities in his early years of observing the various fossile productions in their native beds; and descended the mines of *Derbyshire,* and of some other counties, with uncommon pleasure and observation. He collected with care the products of these countries; and examined them by such experiments, as he had been taught, or had discovered: hence he obtained not only distinct but indelible ideas of the properties of bodies, at the very time when he learnt the names of them; and thus the complicate science of chemistry became not only easy, but delightful to him."

It seems that Charles had inherited stammering from his father and it was the hope that he might be cured by learning French early in life. He was therefore sent to Paris with a private tutor, the Reverend Mr. Dickenson, rector of Blimhill in Shropshire, who was said to have been modest, learned and scientific. During the two years Charles spent with him in Paris no conversation was allowed in English, and Charles returned completely cured of his stammering.

In discussing his son's education, Erasmus gives free expression of his opinion of contemporary pedagogical methods in the following remarkable passage:

"Ye classic schools! ye not only overcome the struggling efforts of genius and bind his Proteus-forms, till he speaks the language you require; but you then divert his attention from the nice comparison of things with each other, and from associating the ideas of causes and their effects; and amuse him with the looser analogies, the vain verbal allusions which constitute the ornaments of poetry and of oratory! . . . Mr. *Darwin* acquired a competent knowledge of the latin and greek languages, chiefly by reading books of useful knowledge, or which contained the elements of science: and which were more agreeable to him than the monstrous and immoral tales of heathen mythology, or of fabulous history. He was of opinion, that to study these dead languages so accurately as to criticise their beauties, and at a time when all their books of real value had been repeatedly translated, was a prodigality of labour, which might suit the retirement of a pedant, but was unbecoming an active philosopher: that to acquire a taste for greek poetry by years of ill-employed industry, was not much more important than to acquire the power of playing well on some one musical instrument: and that, in the schools of language as in the schools of drawing a man of science would learn the use of the pen and pencil, as far as they are concerned in the expression or communication of distinct or useful ideas; but to waste the first twenty years of life in learning the metaphors of language, or the drapery of drawing might serve those, who made poetry or painting a profession; but was liable to disqualify the mind of the more energetic pursuits of business or philosophy."

Erasmus Darwin saw in Charles the following traits which he attributed to his mother's influence and inheritance:

"Nor amid these acquirements of knowledge was his taste for morality neglected; for his ingenious mother, even to her latest hour! instilled into his breast a sympathy with the pains and with the pleasures of others, by sympathizing herself with their distress or exultation; she flattered him into a sense of honour by commending his integrity, and scorn of falshood [sic], before her friends: and taught him prudence by pointing out to him the ill consequences of the bad conduct of others, whose names or persons he was acquainted with: and as she had wisely sown no seeds of superstition in his mind, there was nothing to overshade the virtues, she had implanted."

Charles presumably stayed at the Lichfield school until early in 1775. At all events there is no further record of him until he matriculated at Christ Church in Oxford, and

there the only existing record concerning him is the matriculation entry. It reads as follows:

> "Charles D.
> S. Erasmus of Lichfield W. Staff.
> Ch. Ch. Matriculated 30 March 1775 age 16."
> (Foster's *Alumni Oxoniensis*).

Charles spent nearly a year at Christ Church, but he came to dislike the atmosphere intensely feeling that his mind was going to seed in the pursuit of "classical elegance," and he "sigh'd to be removed to the robuster exercises of the medical schools of Edinburgh."

III. *Edinburgh.*

Charles Darwin went to Edinburgh late in 1775, or early in 1776 and, apart from occasional trips home, he remained there until his death. From a letter to him from his father dated April 2, 1776, one gains the impression that by that date he was well established in the University.

The school of medicine at Edinburgh in the second half of the 18th century was the most vigorous in Europe. Robert Whytt, the professor of the institutes of medicine (physiology) [1747-1766], had a few years earlier discovered the principle of reflex action (1751). The experimental method was also being inculcated in students by his successor, William Cullen [1766-73] and by *his* successor, James Gregory, who was professor of the institutes from 1776 until 1781. Alexander Monro, II, the anatomist, also gave strength and versatility to the school, and added much to the stimulating intellectual atmosphere of the great community in which they lived. It was the Edinburgh of this period that created Benjamin Rush, and others of that virile group which established the medical school of the University of Pennsylvania shortly before the Revolution.

Charles Darwin had the good fortune to become intimate with Andrew Duncan, a rising clinical teacher of the Edinburgh school (professor of the theory of medicine, 1790-1819). Duncan took Charles to live in his house and gave

it is likely that the dissertation on the pulse represents one of his earliest pieces. This document reveals his powers as an observer more clearly than the two published dissertations mentioned above, and it illustrates, incidentally, that he had an excellent grasp of relevant contemporary literature on the heart and circulation. He discusses the causes and significance of the variations in the pulse and gives a clear description of normal variation with age and of the effect of various physiological states such as exercise, rest, eating, somnolence, etc.

No other unpublished manuscripts by Charles Darwin have been found.

Little wonder that the untimely death of such a youth should cause profound regret that found expression in a most surprising variety of channels. The circumstances of his death are described in the following paragraph from an anonymous obituary published in *Medical and Philosophical Commentaries* (Edinburgh, 1778, 5, 329-336).

"About the end of April, Mr. Darwin had employed the greatest part of a day in accurately dissecting the brain of a child which had died of hydrocephalus, and which he had attended during its life. That very evening he was seized with severe head-ach. This, however, did not prevent him from being present in the Medical Society, where he mentioned to Dr. Duncan the dissection he had made, and promised the next day to furnish him with an account of all the circumstances in writing. But the next day, to his head-ach there supervened other febrile symptoms. And, in a short time, from the hemorrhagies, petechial eruption, and foetid loose stools which occurred, his disease manifested a very putrescent tendency. And, notwithstanding the skill of Drs. Cullen and Black, who attended him from the beginning of his affection; notwithstanding the anxious care and attention of his father, Dr. Darwin, a physician of great eminence in England, who arrived at Edinburgh some days before his death, his disease at length terminated fatally."

In addition to three detailed obituaries published within a few weeks of his death, accounts of Darwin found their way into contemporary biographical dictionaries such as Hutchinson's *Biographia medica*, and later into the *Biographie universelle* (vol. 10). Much the most interesting contemporary document, however, is an anonymous poem entitled *An elegy on the much-lamented death of a most ingenious young gentleman, who lately died in the College*

at Edinburgh where he was a student. Only one copy of this has been traced and it was sold in 1931 by Messrs. Blackwell of Oxford to Mr. Paul B. Victorius, then of New York and now of London, who has generously allowed me to have the title-page reproduced and a rotograph made of the text. A manuscript note attributes the elegy to 'Mr. Jackson,' though not identified with certainty, it is possibly Richard Jackson, a prebendary, who was living in Lichfield in 1778, or John Jackson, the historian of Lichfield. There are references throughout the elegy to Charles's early education, his reading of learned authors, his interest in observation of natural objects and to his instincts for collecting.

Dr. Andrew Duncan's affection for Charles Darwin was such that he caused him to be buried in his family vault in the Chapel of Ease of St. Cuthbert's at Edinburgh, now known as the Buccleuch Parish Church Burying Ground. The tablet is the first one on the South wall of this vault and it bears among other things the inscription "He cultivated with success the friendship of ingenious men and was buried by the favor of Dr. A. Duncan in this his family vault."

Such then was the career of the first Charles Darwin, and it would almost seem that Nature, thwarted in her first endeavor, caused another Charles Darwin to see the light of day.

IV. *The Darwins and digitalis.*

One of the remarkable features of Charles Darwin's book is a description of the therapeutic effects of the decoction of foxglove. Nine case histories are given, appended rather casually on pages 103-112 after the following heading: "A note belonging to *page* 65, *and* 68." One would naturally infer that they were cases seen and described by Charles himself, for there is nothing, except their position in the text, to suggest that they were inserted by his father. They are prefaced by the following sentence: "The foxglove has been given to dropsical patients in this country with considerable success: the following cases are related

with design to ascertain the particular kinds of dropsy, in which this drug is preferable to squill, or other evacuants." The case-reports are important since they contain the first accurate description of the therapeutic effect of digitalis in cardiac oedema published in any language, antedating Withering's celebrated book, *An account of the foxglove*, by five years.

The question arises whether these cases were described by Charles or by Erasmus. There is no direct statement in the book, but the evidence is overwhelmingly in favour of their having been appended to Charles's thesis by his father. In the *Medical Transactions* of the College of Physicians (London) for 1785 (vol. 3, p. 258) Erasmus Darwin says, "In a pamphlet entitled 'Experiments establishing a criterion between mucaginous and purulent matter, with an account of the retrograde motions of the absorbent vessels,' printed for Cadell, 1780, I subjoined about half a dozen cases of dropsies treated successfully by the decoction of *digitalis;* and endeavoured to distinguish the species of dropsies, in which it would generally succeed. To that account I could now add at least a score of other cases, cured by the same method, of those kinds of dropsy, the seat of which is supposed to be in some part of the *thorax*, and which is attended with *anasarca* of the limbs."

Though Erasmus Darwin was inclined to be unscrupulous, there is scarcely reason to believe that he would claim for himself work that had been done by his son. In the *Zoonomia,* published in 1794 (vol. 1, p. 326), a similar reference is made to his having appended a description of cases treated with foxglove to his son's thesis. Granting then that his statements are accurate, how did it come about that he used and described the effects of digitalis before Withering's celebrated book was published?

Erasmus Darwin has two definite claims to priority in publication: the appendix to his son's thesis which appeared in 1780, and the second paper which was dated Jan. 14, 1785, and read March 16, 1785, bearing the title "An account of the successful use of foxglove, in some dropsies, and in the pulmonary consumption," which as

already mentioned, appeared in the *Medical Transactions*. This paper seems to be little known, and is not referred to by Withering. Well described case reports are given with many more details in each one than had been included in the account of 1780. All the classical symptoms are mentioned, and it was evidently Darwin's practice to push the drug until it produced symptoms of nausea and diarrhoea. Darwin was not the incisive clinical observer that we find in Withering, but his descriptions are not without great merit. His critical faculties were less acute than those of his Birmingham contemporary, and they allowed him to recommend the drug for pulmonary consumption.

Nowhere in any of Darwin's writing on digitalis is Withering's name mentioned, and there is no explanation of how he came to use the drug. The first case in his appendix of 1780 was evidently seen in consultation with Withering, for it is recorded in Withering's book as Case No. IV. Here one finds the probable explanation of Darwin's use of the drug.

It is clear from one case report that Withering was annoyed with Darwin for having published a somewhat garbled and incomplete account of the case which they had seen in consultation. Withering's reference stating that Darwin had trusted to his memory for the details of the case are largely, but not entirely, correct for one finds in Darwin's *Commonplace book* (unpublished, p. 8) the following entry:

> "Miss Hill of Aston near Newport on July 1776 had been indisposed sometime and was then seized with a cough and afterwards a spitting of digested mucus . . .
> "R Fol. Digitalis."

No mention is made, however, of having seen the case with Withering.

Withering's testimony, however, is clearly correct, that Erasmus Darwin first became acquainted with the action of digitalis on the 25th of July 1776 when seeing Miss Hill in consultation with him. If one applies modern standards of ethics one must conclude that the grandfather of the

celebrated naturalist was somewhat unscrupulous. If priority of publication means anything in these circumstances he indeed has a legitimate claim over Withering. However, one must recognize that it was Withering, and not Darwin, who convinced his medical contemporaries, and it was he who inaugurated the systematic use of the drug; he kept full records of his results, and published after an interval of ten years of careful observation, a full and systematic treatise on its action. Withering's preface is dated "Birmingham, 1st July, 1785." The book itself, presumably appeared sometime in the autumn of that year.

Charles Darwin is mentioned only once in Withering's book, but the passage bears out our inference concerning the likelihood that Erasmus Darwin had informed his son of the action of digitalis. On page 8 Withering states:

"I am informed by my very worthy friend Dr. Duncan, that Dr. Hamilton, who learnt its use from Dr. Hope, has employed it very frequently in the Hospital at Edinburgh. Dr. Duncan also tells me that the late very ingenious and accomplished Mr. Charles Darwin, informed him of its being used by his father and myself, in cases of Hydrothorax, and that he has ever since mentioned it in his lectures, and sometimes employed it in his practice."

Summary.

The evidence which I have just summarized establishes priority of publication concerning the action of digitalis for Erasmus Darwin, but on every other ground, Withering deserves full credit for the discovery. Charles Darwin, the medical student, had been informed of its action by his father and had attempted to account for it on the basis of improvement of lymphatic drainage. But the work, accomplished by the first Charles Darwin is less significant than the abundant evidence of his intellectual ability and precocity, and I have ventured to lay the details of his career before you because of their intrinsic interest and in the hope that the information will serve in a small way to clarify the unsolved problem of the relation of nature to nurture in establishing mental traits and capacities.

COMMITTEE ON PUBLIC HEALTH RELATIONS

REPORT ON VITAMIN D MILK

The City Department of Health requested the opinion of The New York Academy of Medicine relative to the desirability of making energized milk generally available, and the character of Health Department regulations governing the production and sale of such milk.

A subcommittee was appointed to study the various phases of the problem, and the following is the report prepared by the Subcommittee and adopted by the Committee on Public Health Relations.

Reasons for Vitamin D Milk

It has been satisfactorily demonstrated that in order to prevent rickets, children, particularly during the first year of life, require Vitamin D, in addition to that supplied by the usual foodstuffs. Its administration in terms of fish oils is frequently difficult, although these oils are potent and contain easily available D. Administration by means of irradiated ergosterol and other such substitutes for oil is also at times difficult because of taste and gastric intolerance, and is unsatisfactory because of the lessened availability of the contained D. The inclusion of Vitamin D as an integral part of some palatable food, such as milk, removes these objections and assures ease of administration. Moreover, milk is the universal food for infants; carries with it other vitamins; represents in itself the balanced ration; is rich in calcium and phosphorus; and is an important part of the diet during the period when additional D is most needed.

Methods of Producing Vitamin D Milk

Several processes have been developed for concentrating the active vitamin found in cod liver and similar oils. One of the earliest of these, the Zucker process, is now commercially employed to supply additional D units to food, especially to milk.

The commercial concentrate has 1,500 to 1,800 times the Vitamin D content of the Steenbock standard cod liver oil. After being tested by biological assay at the place of production, it is diluted to a standard strength of 150 D (i.e. 150 times the Steenbock standard cod liver oil, or 195 rat units per gram) and sent to the milk distributor. At the milk plant the material (commercially known as Vitex) is again diluted in a can of milk and then distributed into the large supply vats containing measured quantities of raw milk where it is thoroughly mixed and then sent to the pasteurizers. The dilution ratio, standardized concentrate to milk, is about 1:1,200. The total dilution ratio, full strength concentrate to milk, is about 1:12,000. If desirable the standardized concentrate can likewise be made up in a milk dilution so that the latter figure represents the dilution of added foreign substance. Under the plan of distribution at present adopted, samples of the finished product taken in the market are assayed regularly by a University, State Board, or other equally satisfactory laboratory at the expense of the concentrate manufacturer and under the scientific direction of Dr. Zucker and a faculty committee of Columbia University. At the present time about 100 such assays per month are reported from the various laboratories of which about 60 are from milk supplies.

With continuously increasing market demand for preparations of this sort, greatly enhanced by a large demand for a second grade product used in chicken feed, it has been possible to improve the processes of concentration, to elaborate the procedures of biological control, and, by selection, to improve the quality and the uniformity of the first quality product destined for human consumption.

With the discoveries by Steenbock and by Hess of the influence of ultra violet light of certain wave lengths upon ergosterol, and other organic compounds, a second important source of Vitamin D became available and developments in this field have been extensive and rapid. With regard to milk supplies there have been two particular

outcomes of this work, namely, the feeding of cows with irradiated commercial yeast or ergosterol; and more recently, direct irradiation of the milk itself. The latter process has been extensively investigated as to its clinical, electrical, optical and mechanical details and in particular as to chemical changes in the milk itself. It has been found necessary to limit the time of exposure to a few seconds or to make a corresponding decrease in the intensity of the light in order to avoid unfavorable taste-producing reactions upon the milk fats. The carbon arc lamps produce a high concentration of ozone in their immediate neighborhood and special ventilation provisions have to be made to prevent contact of the milk with this substance which likewise reacts on the fats disadvantageously. The antirachitic potency is imparted to the milk rapidly without appreciably affecting Vitamin A and slightly Vitamin C.

Each of these systems of treatment has its specific mechanical and economic advantages. For the small dealer the avoidance of expensive equipment and the ability to mix up from day to day the exact daily requirements of treated milk are controlling items. To the large distributor, there is claimed at the present time for the process of irradiation an actual overall economy despite a rather heavy initial outlay. The situation has not however been sufficiently developed to justify any direct comparison of costs at the present introductory stage.

The concentrate method enjoys the undoubted advantage of flexibility in that dosages of any required quantity can readily be introduced so that milks could, if desired, be put on the market with differing concentrations for specific purposes. The mechanical operations of the two processes at the plant are perhaps about on a par although the actual operations of homogenizing and mixing are quite familiar to milk plant operators. Here again however it is only fair to await developments and satisfactory evidence that proper control mechanisms have been produced.

Physical, Biological and Clinical Tests

There has been some uncertainty and there are certain conflicting opinions upon the question of the rat unit as a criterion of rickets prevention efficiency in the human infant and the facts in this matter must be established before there can be any satisfactory therapeutic use of Vitamin D preparations of various types. This difficulty, however, is a general one not specific to the milk problem and, in view of the flexibility of the concentrate method at least, offers no insuperable difficulty since any specified dosages are readily obtainable. Under the irradiation procedure as now managed it does not seem to be feasible to obtain a much greater concentration than between 50 to 60 rat units per quart.

From the point of view of sanitary production and of administrative details the two systems are about on a par. The concentrate itself is an anhydrous oil which appears to be bacteriologically sterile as would be anticipated from the method of its production. Being added to the raw milk before pasteurization it introduces no serious sanitary problem. The irradiation procedure likewise is from this point of view similar to other milk handling procedures and is likewise safeguarded by subsequent pasteurization. The somewhat technical point, the addition of a foreign substance to the milk, can be practically avoided, if necessary, by diluting the concentrate in pure milk fat or as is now being experimentally tested, by the use of an evaporated milk as a diluent. Any fortification of natural milk with Vitamin D obviously involves certain additions and chemical alterations in the milk and any milk so modified should be properly labelled to comply with basic pure food laws. If such fortified milks are desirable and are to be approved by the board of health, it is rather quibbling to raise the point of an added foreign substance against either of these two processes.

In the milk of yeast-fed cows there may be considerable variation in the number of rat units per quart, which is due to the difference in the amount of irradiated yeast fed

daily. The potency of the milk depends almost entirely upon the amount of irradiated yeast given and one can conclude that if there is any great variation in the potency of milk of cows fed in this manner, there has been some error in the amount of yeast given to the cows.

As important as the content is the degree of utilization of the Vitamin D. By clinical test this is found to be protective in fortified milk when 24 ounces containing 40 units, are given daily. On the other hand, Kramer and Gettleman believe that unit for unit, there is no difference in the action of directly irradiated milk or milk from cows fed irradiated yeast.

Furthermore, Hess and Lewis (*J.A.M.A.*, July 15, 1933) clinically appraised·medicinal oils containing 40 units per gram—"3D"—and found the prophylactic base to be 250 units of cod liver oil D. This work seems to indicate that the availability of D in irradiated milk is five times that of the D content in medicinal oil.

One of the most interesting problems in the therapeutics of rickets is the discrepancy between the rat unit content and the clinical efficacy of various anti-rachitic agents. For example, according to Hess and Lewis, 42 rat units (Steenbock) in the form of irradiated milk, bring about a rapid cure of infantile rickets, whereas 80 units of milk from yeast-fed cows, approximately 160 to 240 units of cod liver oil, and 600 to 800 units in the form of viosterol, are necessary to accomplish a similar result. The ratio of effectiveness of irradiated milk, yeast milk, cod liver oil and viosterol, is therefore, from the point of view of rat units, approximately 15:8:4:1. As a result of these experiences it is impossible to predict the clinical potency of a new anti-rachitic agent merely from its rat unitage. The dosage of new agents can be accurately determined only by experiences in the clinic.

On the basis of the already rather extensive evidence it is safe to assert that Vitamin D milks, irrespective of the manner in which they are produced, are capable not only of preventing but also of curing rickets. If all artificially

fed infants were given Vitamin D milk, rickets would become a rare disorder. It should be noted, however, that occasionally infants will develop rickets in spite of receiving a liberal supply of Vitamin D. These cases are often resistant to treatment with even excessively large amounts of Vitamin D, and should they be encountered in infants receiving Vitamin D milk, it should *not* be deduced from such an experience that the fortified milk has proven to be a failure.

There are at present four designations for units and three different strengths and there is need of uniformity in gauging the curative and preventive potency of the Vitamin D milk for clinical use as well as for health administration purposes.

The assay of the D content of such fortified milks has been time-consuming and expensive. When stated in terms of rat units, the D value must be translated into clinical units and the values of the various forms of D carrying material can not be considered as interchangeable.

Biological assay of energized milk consumes three weeks and provides information too late for practical value.

The most critical detail, however, is the control of the character and intensity of the illumination to secure a uniform and predetermined concentration of the vitamin in the milk. Some very excellent apparatus has been developed for measuring and recording the energy output of the radiating lamp in a certain limited range of the spectrum. It may safely be assumed that these instruments will produce accurate records. The following further assumptions are necessary, however, to justify the acceptance by the administrative officials of any such record as a criterion of Vitamin D productions:

(a) The effectiveness of the various wave lengths of ultra violet light in their ability to produce Vitamin D is paralleled by their respective powers to excite the photoelectric response in the measuring apparatus.

(b) The formation of Vitamin D in milk is a function only of the incident radiation and not of such other physical conditions as temperatures of the milk, chemical composition, etc.

(c) The mechanical details of the operation which determine the time of exposure of the milk to the rays, the thickness of the exposed film, etc., have been so perfected that these important factors may be safely considered to be held constant.

Item (a) has been established by controlled experiment with a reasonable degree of approximation for the limited conditions of the tests. The other items have received only secondary mention.

This indirect test may be capable of complete and satisfactory standardization and would, if so standardized, be of the greatest assistance in the administrative control of the product of Vitamin D milk. Its acceptance for this purpose however must await the most thoroughgoing study of its true significance and during this introductory stage any new installation should be subjected to an extensive over-all calibration of the physical measuring device against the actual anti-rachitic potency of the milk.

Vitamin D Milk for General Consumption

In regard to the question of the possibility of toxic effects resulting from Vitamin D milk, it may be of interest that no one has ever observed any untoward symptoms or hypercalcemia resulting from its administration. It seems that the low titre of rat units in energized milk would preclude such a possibility. Furthermore, feeding rats 10,000 times a therapeutic dose of Vitamin D milk for a period of months did not bring about any deleterious effects, or any abnormal histological changes in the tissues. On the other hand, the need of additional D for well adults is not satisfactorily proven. There is evidence indicating the advantage of additional D in conditions associated with low calcium, in dental caries, during parturition and lactation, perhaps in chronic bone disease and possibly in tuberculosis.

The advisability, therefore, of universal or general energizing of milk does not seem apparent.

Administrative Problem

Assuming that the need for Vitamin D milk has been established, the question then arises as to the responsibility, if any, of official governmental agencies for the regulation and control of the production, handling and sale. This is a question which the committee has considered only because it has been advised that the health departments of the state and the city of New York would welcome an expression of its views.

Apparently neither the State Public Health Council nor the New York City Board of Health has yet undertaken to establish detailed requirements in their respective codes. The State Sanitary Code contains the brief definition that "The term 'Vitamin D milk' means milk in which the Vitamin D content has been artificially increased" and the general provision that it must be made from milk meeting the applicable requirements of the code for milk sold under grade designation. The committee is informed that the question of the need for additional and more specific requirements has been considered by the State Department of Health and the Public Health Council in the recent past and it has been felt that it would be unwise to establish more specific or detailed requirements while the production of Vitamin D milk is still in an experimental stage and until the various scientific and administrative problems involved are better understood.

The State Department has taken the tentative position that it would neither endorse the product nor interfere with its sale so long as it conformed to the above mentioned general requirements. It has felt that this "neutral" position was justified in view of the apparently well founded claims as to the need among children for the product and inasmuch as the possibility of harm resulting from its sale was very remote, providing the milk used was of safe sanitary quality.

It would seem that the principal immediate administrative problem, from the standpoint of protecting the public, is that of assuring that Vitamin D milk sold actually contains the amount of the vitamin which it is represented to contain. It would seem that the health departments, having jurisdiction in matters relating to the sanitary quality and healthfulness of milk, would be the logical agencies to assume such responsibility, so far as it is practicable. From the above discussion it is apparent that the problem is not a simple one. The question of the relative merits of the three available units of measurement is still not completely settled. There are still differences of opinion as to the effectiveness per "unit"—depending on the unit selected—of the vitamin as added by different processes and pending further clinical experimentation it does not seem desirable as yet to form definite conclusions as to what the minimum acceptable standard amount of the vitamin per quart of milk should be. The laboratory procedures required to determine the amount of the vitamin in a specific quantity of milk are involved and expensive and thus far have been undertaken in only a few laboratories, including those maintained and operated for commercial purposes. In view of the expense involved it would not seem to be feasible, under present conditions, for health departments to attempt to set up and finance independent official laboratory service to carry on this work, especially considering the fact that the sale of Vitamin D milk is still limited and that the product is in a sense proprietary.

Involved in the public health aspects of the matter is the question as to what, if any, hazard is involved in the addition of a foreign substance to milk, as is necessary in one of the recognized procedures for increasing the Vitamin D content. While it may be "splitting hairs," the general feeling seems to be that the indirect addition of Vitamin D to milk through irradiation and through the feeding of irradiated yeast to cattle need not be considered the addition of a foreign substance in the commonly accepted sense but that this can not properly be held to apply to the addition of a definite physical substance, as in the case of the

Zucker cod liver oil concentrate. The committee feels safe in venturing the opinion that, considering the fact that this concentrate when it leaves the manufacturer is practically a sterile product, the fact that the amount added to milk is small and the further fact that the procedure involved in adding the concentrate to the milk by the distributor is one not requiring contact with human hands and offering little opportunity for contamination, the hazard, if any, would be so slight as to be negligible, providing the milk was pasteurized after the addition of the concentrate.

Looking at the matter purely from the standpoint of medicine and health, the committee at the moment is unable to see any valid objection to permitting the addition of Vitamin D to milk by any of the recognized methods, under properly controlled conditions.

In view of the fact that the production of Vitamin D milk is still experimental, that existing methods may be changed or improved and, conceivably, new methods may be evolved; that the relative values of units of measurement and the basis for establishing minimum standards for Vitamin D content are still unsettled; and in view of the limited availability of laboratory service for the purpose of making assays, the committee is inclined to feel that the official health agencies in the State and in the City of New York would be acting wisely if they continued, for the present, to defer the enactment of detailed and specific requirements beyond those necessary to assure that the ultimate product be of a safe sanitary quality.

The committee therefore is of the opinion that Vitamin D milk, produced by any one of the three methods, should be allowed to be sold, the containers to carry a label to the effect that it is Vitamin D milk, indicating also the process used. As to whether or not health regulations should require that the label specify that the milk contains a certain specified minimum number of protective units, say 50 per quart, is a matter with regard to which there is still a considerable amount of difference of opinion.

Theoretically, it would be desirable for the producers to state on each bottle the number of units of Vitamin D present in the milk, but in view of the fact that health departments have no laboratory facilities for assaying milk, it is questionable whether this requirement would be practicable. It might perhaps, for the time being at least, be more desirable that the label merely state the source of Vitamin D in each instance, the health department to decide what it considers a normal protective dose and in its license provisions demand proof from time to time that the milk produced under the license contains the stated dosage.

From the evidence now available, the Committee is of the opinion that such requirement will be satisfactorily fulfilled by

1. Directly irradiated milk containing 56 rat units per quart.

2. Concentrate milk and yeast-fed milk containing 100 rat units per quart.

This report was prepared by a special subcommittee consisting of:

Herbert B. Wilcox, *Chairman*
Paul Brooks (Albany)
J. M. Lewis
Edgar Mayer
Earle B. Phelps
E. H. L. Corwin, *Secretary*

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Madame Curie remained throughout her life a woman of simple tastes and modest requirements. She received her numerous honors with graceful reserve, but full appreciation. She was extremely direct and simple in her approach to every problem. She was always ready to discuss freely any subject in which she felt herself competent, but was chary of speculations and predictions. In her death passes one of the most cultivated feminine minds and distinguished investigators in the history of science.

JAMES EWING.

DEATH OF FELLOW OF THE ACADEMY

LEALE, MEDWIN, B.A., M.D., 555 Park Avenue, New York City; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1896; elected a Fellow of the Academy December 3, 1908; died, June 30, 1934. Dr. Leale was a Fellow of the American Medical Association, a member of the County and State Medical Societies, The Pathological Society, the Roosevelt Hospital Alumni Association and the Alumni Association of St. John's Guild. He was Consulting Physician to St. John's Hospital in Brooklyn, Nassau Hospital in Mineola, and North Country Community Hospital in Glen Cove.

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EDITORIAL

THE MEDICAL HISTORY OF ROBERT SCHUMANN AND HIS FAMILY[1]

In the old Leipzig inn called The Coffee-Tree (Kaffeebaum), there sat of evenings, through the thirties of the 19th century, a pleasant mannered young fellow, of handsome appearance, attractive mien and enthusiastic nature, who reigned, in his chosen corner of this charming hostelry, as the leading spirit of a new departure in music. This was Robert Schumann, a man of unique genius, destined to become the prime-mover of music under the romantic tradition, the ablest critic of his art in his period, and one of the best beloved of all the great composers. Well-born, well-nurtured and well bred, he came of a family of Thuringian landowners, who settled eventually in Saxony. His paternal line numbered several clergymen, but in the Leipzig of Schumann's prime, which had supplanted Frankfurt as the center of the Continental book-trade, most of his people had gone over to the book business. His father was, in fact, a clergyman turned book-seller, a pursuit which had been followed by all his maternal uncles. His mother, the daughter of a Bohemian surgeon, had latent in her composition, no doubt, the Czech passion for music; for there is no evidence of any musical interest whatever in the Schumann strain. If there be anything in the Goethe-Scho-

[1]Read at meetings of the Johns Hopkins Medical History Club, February 15, 1932; the College of Physicians of Philadelphia, October 10, 1932; the Charaka Club (New York), November 15, 1933, and the Goethe Society, Baltimore, Md., January 20, 1934.

penhauer view of the inheritance of mental traits,[2] Schumann's musical genius came from the spindle side of his house. In one member of a collateral branch of the Schumann family, there was a solitary instance of suicide. The young Schumann himself was of jolly, loveable, easy-going nature, a natural gentleman of refined disposition and artistic tastes, bred to the law but inclined to neglect it, out of his unbounded passion for music, which had singled him out, as a Mendelian sport, among the solid, respectable, withal prosaic sibs of his paternal and maternal stock. A dispute with his widowed mother as to his fitness for the musician's calling was inevitable, and after some argument, he was permitted to take up advanced piano technique and composition under Friedrich Wieck, at that time one of the leading music teachers of Germany. Wieck, a man of bigoted, pedantic character, with an effective pedagogic method, proved an able instructor withal, whose Spartan rigors of discipline were visited mainly upon his young daughter Clara, with a single eye to making her a great pianist. As sometimes happens, in training musical talent of an unusual order, fortified by initial firmness of character, he succeeded, as did Mozart's father, beyond the dreams of avarice. At the age of nine, Clara was playing Mozart's E flat concerto to the delight of a Leipzig audience and, two years later, made her first public appearance in the exclusive concerts at the Gewandhaus. For this she received 30 thaler, of which 20 were turned over to her watchful parent. About the same time, there appears in her diary the first mention of a certain Herr Schumann, "who has been living with us as a pupil in music since Michaelmas." The two young people are soon rollicking playmates, as well as fellow students in counterpoint under Wagner's teacher, Theodor Weinlig, the old cantor of the Thomasschule. At thirteen, Clara is a sprightly, cheerful, dark-eyed, little elf, so ignorant of the life around her that

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2 *Vom Vater hab'ich die Statur,*
Des Lebens ernstes Führen,
Vom Mütterchen die Frohnatur
Und Lust zum Fabuliren.
Goethe.

she cannot tell ducks from geese, albeit her maiden effort in composition, a processional of swans (*Schwäne kommen gezogen*), was launched at the age of eleven. Even so, she has already known sorrow, through the separation of her parents, and is destined to further experience of it when she learns of her friend's engagement to the daughter of a Bohemian nobleman; for Schumann's mother, with an intelligence unusual in the maternal mind, had already drawn the child to her with the hint: "You must some day marry my Robert"; and was thus dubious about the ill-considered Bohemian engagement, soon destined to be broken off. At sixteen, Clara is an attractive, active-minded brunette of gentle features, strong compelling eyes, sensitive mouth, friendly, bitter-sweet smile, gracious mien and unstudied ease of manner and movement; of whose playing the great Goethe observes that "this girl has more strength than six boys"; and Mendelssohn that she rendered his B flat Capriccio "like a little devil." In brief, a very genuine, upstanding bit of piquant femininity, liked by everybody, and whose engagement to her old playmate is now a foregone conclusion. About this engagement to a man nine years her senior, Papa Wieck is nowise enthusiastic. He regards the making and breaking of Schumann's earlier engagement, humiliating to his daughter in itself, as an index of lack of character; questions Robert's ability to support a wife and grudgingly withholds consent until the fantastic youth can produce legal evidence to that effect. This leads to a protracted engagement, with many ups and downs, culminating in a lawsuit, which brings the sentimental relation of Robert and Clara into pitiless publicity all over Europe. At this time, Schumann had already made his mark as one of the most promising original and gifted composers of romantic Germany; but he had, at the same time, annihilated his future as a concert pianist by abuse of a mechanical contrivance designed to strengthen the weak fourth finger, but impairing its efficiency forever. The lawsuit is eventually won and the young couple are married in 1840; but Schumann's outlook on life is already clouded by morbid introspection, effect of worry over the publicity

attaching to his engagement and the permanent handicap of his finger dexterity, which gives to his piano music a certain strange physiognomy. That the impact of worry of this kind, upon a nature essentially noble-minded, may superinduce the autistic or shut-in life, is beyond question. Nevertheless, this turns out to be one of the happiest marriages ever made between people of artistic endowment, lasting without a break, up to the composer's untimely death, and the activator, in his case, of sixteen years of most astounding productivity. Masterpiece after masterpiece he pours out, with a facility rivalled only by the great of old; and the source of his inspiration is ever his wife, whom he surprises from day to day with some novel stroke of genius. The quality and originality of this music make it a thing apart. As with Rheingold or Tristan, it is like nothing ever heard before; and was destined to exert a lasting influence upon the later men, from Brahms and Richard Strauss to Jensen, Kirchner, Grieg, Dvorak or even Debussy. From such clever initial *pastiches* as the Papillons or the Carnevale, Schumann pyramids with ease up to such masterpieces as the C major Fantasie, the piano concerto, the piano quintet (a glorification of his artistic life), the songs, the Peri, the Manfred, the Spring and Rhineland symphonies; and these things, among the finest expressions existent of the inner life of humanity, have enshrined the memory of the composer with an aureole of affection, comparable with that accorded to Oliver Goldsmith or Charles Lamb in English literature. To know the music is to love the man. The gentle prime-mover of all this enchantment is Clara, who, like Minna von Barnhelm, prides herself upon her Saxon strength and fidelity (*ein starkes Mädchen*), becomes, in fact, the business manager of this household, which she finances by teaching and giving concerts, while Robert dreams away his days at the piano or in his Kaffeebaum corner, reluctant even to make himself known to the extent of accompanying his wife on concert tours into Russia or the Netherlands. An inspiring writer, an influential journalist, a discerning critic, he is but an indifferent orchestral director, prone to lose the

count and dislocate rhythm by lapsing into reverie; and so loses his position in Düsseldorf. This and other setbacks begin to prey upon his mind. For the first time in his married period, this gentle housefather scolds his devoted wife, an abrupt change, noted even in the Hippocratic Canon as ominous. As time wears on, Schumann becomes more and more sensitive and autistic, inclined to live within himself and sit mumchance, without uttering a syllable, in social gatherings. Presently there develops a strange humming in the ears, upon a single note, intensified and prolonged up to excruciating agony, with insomnia, set off by audition of music more heavenly than he had ever dreamed. On a fateful morning (February 27, 1854), he rushes from the house in scanty attire and throws himself into the Rhine. His life is saved by the captain of a nearby vessel and he is brought back home by masqueraders, returning from nocturnal festivities. He is pronounced insane, and is committed to asylum, living on for two years, with rare lucid intervals, to die on July 29, 1856 at the age of forty six. The autopsy shows, among other things, certain spicules of cranial bone, impinging upon the brain and lacerating the cerebral membranes. The brain is one of the smallest and lightest on record in the medical histories of men of genius.

Fortunately for Clara, there had appeared, just upon this grim break-up in her life, a young spirit, stronger even than herself, who was providentially fated to be the friend in need and her bulwark against despair. Brave with the courage of the gentle (the faithful Mendelssohn long dead), the unhappy woman now faces life alone, with the additional responsibility of supporting a large family, but not entirely unfriended. Johannes Brahms, whom Schumann, with the insight of true genius had hailed as the coming composer, the continuator of the great Bach-Beethoven tradition, is at this time a light-hearted, blond, blue-eyed boy, long haired, like *crinitus Iopas* in Virgil, touring the Rhineland in search of opportunities, with hardly a penny in his pocket. He happens in upon the Schumanns unannounced, if not entirely unbidden. At the piano he astounds

them with the virile fire of his execution and the originality of his conceptions. As he plays, his young Raphael face is transfigured with the light that never was on land or sea. In the dire poverty and hardship of his childhood, he is like unto Schiller.[3] He has even eked out a living on occasion by playing in the lowest sailor's dives; but the sea-air of Hamburg is in his veins and he is already winning up to manhood unscathed. His gratitude to his new friends is unbounded and through the long tragedy of Schumann's illness and beyond it, he stands by the stricken family, *"als kleiner Mann,"* collaborating with Joachim in getting up concert tours for Clara, albeit penniless himself. Naturally the boy falls in love with her, now a handsome woman in her prime; but here, his mordant sense of humor collides with his feeling of utter helplessness and sorrow over the tragedy of Schumann's fate, to produce the spiritual conflict which he welds into his great D minor concerto. By this token, Brahms attains to the sterner stuff of which manhood is made, surely one of the best men who ever lived upon earth. Clara takes up concert touring in England and becomes at once a perennial favorite with the English people, to whom her sadness seems "so pitiful." Like the devoted mother in the Spoon River Anthology, she raises her little brood up to the self-supporting status, ranking with Essipoff and Sophie Menter as a concert performer, up to her retirement (aet. 59), as teacher in a conservatory at Frankfort on the Main. Her essential service is that along with Brahms and Joachim, she has made the better sort of music a going concern on the concert stage, supplanting the vapid Liszt-Thalberg tradition of meretricious variations, operatic fantasias and salon music of affected mien. The native fire, which had rivetted Goethe and Mendelssohn, remains the essential trait of her being to the last. Even to a late American observer, she seems, in playing Bach, as if "crowned with diamonds." Brahms remains

[3] As commemorated in the verse of Emanuel Geibel:

"Ein armes Dach nur war's im Gau der Schwaben,
Dort wo der Geniusengel segnend eingekehrt,
Der Sorge Wohnsitz die den blonden Knaben
Früh lehrte wie man duldet, kämpft, entbehrt."

the faithful friend and advisor of the family to the end, surviving her death by less than a year.

Eight children were born to the Schumanns, of whom one died in infancy. The fate of the remaining seven is of considerable interest, as a phase of the biological investigation of family histories (*Familienforschung*), which is now a going concern in Germany.[4] Genealogy and family-trees, from the tables of Egyptian and Sumerian Kings to Burke's Peerage or the Almanach de Gotha, are as old as the hills; but the pace in the utilization of family records was set by the novelists. A favorite theme of the English masters of fiction, from Richardson, Fielding and Smollett to John Galt, Thackeray (The Newcomes) or Galsworthy (Forsyte Saga), has been the life-history of one or more familial groups, centering around the fortunes or adventures of some particular member. This plan was carried out on a grand scale by Balzac, whose *Comédie humaine* covers a whole cross-section of French society in his period; and latterly by Zola (Rougon-Macquart series) and Marcel Proust (*À la recherche du temps perdu*). Familiar examples of more recent vintage are Thomas Mann's Buddenbrooks, Hergesheimer's Black Pennies and The Orissers by L. H. Myers.

Assuming that Schumann's genius was the resultant of a favorable constellation of Mendelian factors and that Clara came by her pianistic talent through her father, one would expect a natural outcropping of musical ability in the children. As a matter of fact, none of the Schumann children had any particular musical gift. Such ability in piano playing as the daughters possessed was largely environmental, the result of careful training given them by the mother and by Brahms. The working out of Mendelian principles in the little family is exhibited along quite different lines and in a significant and striking way. Of the Schumann children:

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[4]For the genealogy of the Schumann family, see: Stammbaum Robert Schumanns. *Veroffentl. d. Schumanngesellsch.*, Zwickau, No. 3. For the life-histories of the eight children, *see*, Memoirs of Eugenie Schumann, London, W. Heinemann, 1927.

1. Marie, the eldest, born on September 1, 1841, contravenes the theories of Karl Pearson and Still about the handicap of the first-born. Far from being a weakling, she was the strongest and most enduring of the entire family, in every respect the flower of the flock. Tall, upstanding, thoughtful, serious, dignified, she inherited the mother's fine dark eyes, an index of her firm, capable character. Endowed with no outstanding musical talent, she became by dint of application, a very capable pianist, often assisting her mother in concert performances for four hands or two pianos. As being the eldest child, and her father's favorite, she was destined to be her mother's regimental adjutant and handy man in running the family after the great disaster. "In spite of your equanimity," said her sister, "you had a distinct tendency to *furor teutonicus,* which would break like a thunderstorm and as suddenly pass. You were also the thoughtful one of the family . . . You were never really happy unless you took care of our mother and us from morning till night, and of many others as well." Strong and sturdy, Marie surpassed her mother's longevity of 76 by 14 years, dying at the age of 90.

2. Else, the second child, born on April 25, 1843, was tall, slender, strongly built, blue-eyed, fair-haired and strong featured. She inherited her mother's sturdy independence, self-confidence, self-possession and tendency to strike out for herself. She left the family early to teach music upon her own, and while possessing no more native talent than thousands of cultivated amateurs in Germany, she became a very competent pianist, capable of replacing her mother in chamber music on the slightest notice. In 1877, she married Louis Sommerhoff, a prosperous American merchant, had four sons and a daughter, and in 1927, was still living at the age of 85. The names of her descendants may be found in the New York City Directory.

3. Julie, born March 11, 1845, was blonde and perfectly normal, like all the other daughters. In 1868, she married an Italian nobleman, Count Marmorito, had two children and died in childbirth in 1872 (aet 27).

4. Emil, born February 8, 1846, died in 1847 of glandular fever.

5. Ludwig, born, January 20, 1848, was dark and strongly built, like his mother, but gloomy, sensitive, introspective and clumsy in movement. He became insane at the age of 22, was confined to asylum for 31 years and died in 1900 (aet. 52). Here the Mendelian recessive in the Schumann strain became dominant, duplicating the father's fate.

6. Ferdinand, born July 16, 1849, was dark-haired and blue-eyed and inherited his mother's practical business ability. Educated at Berlin, he went into business early, became a bank official and married the daughter of a landed proprietor. Military service in the winter campaign of the Franco-Prussian war brought on a rheumatic seizure, intensified during militia service ten years later. Committed to hospital in Berlin, he acquired the morphine habit through the carelessness of an unscrupulous doctor, lost his health and his competence, and died in 1891 (aet. 49), leaving six children on Clara's hands.

7. Eugenie, born December 1, 1851, resembled the mother in sturdiness and competence. She became a music teacher, wrote the memoirs of her family, and is still living at the age of 83.

8. Felix, born June 11, 1854, shortly after his father's break-down, was good-looking, attractive, of artistic bent, author of poems which Brahms set to music, and himself determined to be a musician. The development of lung trouble precluded this possibility and he took up law. Passing his examinations brilliantly, he became a dashing Heidelberg student in cerevis, riding habit and boots, but died prematurely of tuberculosis at 25.

Of the four girls of the Schumann family, three (Marie, Else, Eugenie) lived longer than their mother and it is possible that Julie, who died in childbirth, had the same superior longevity *in posse.* Of the four boys, three (Emil, Ferdinand, Felix) died early of those intercurrent dis-

eases which, in the phrase of Chalmers of Glasgow, "strike laterally," while Ludwig was singled out as the victim of vertical incidence of a Mendelian recessive (insanity). In respect of longevity, the girls were in the trend of the mother's biological fate and even outpaced it; the boys were, all of them, shorter lived than the father.

It remains to say something about the declining years of the two people who made the raising of these seven children possible. The mother, a good disciplinarian, lived among her children as a kind of big sister, signing her letters to them *Mutter Clara*: in other words, she had grasped the true military significance of leadership and "discipline," not to bully but to make them disciples of Clara. In piano training, she followed her father's device, to get a beautiful intonation from the keyboard by pressure rather than by percussion. Brahms was a pioneer in loosening the stiff wrist, with a single eye to autonomy of the ten fingers as individual voices, say in an intricate Bach fugue. Some of the puzzle-headed exercises which he wrote out for the Schumann children were later incorporated in his *51 Uebungen*. The hardships of his childhood and youth, the icy coldness with which music so original as his own was at first received, superinduced in Brahms the usual defensive reaction of a sensitive nature:[5] he was occasionally brusque under gratuitous criticism, even with Madame Schumann; for which he was sometimes vigorously rated by her young daughters. But for Brahms, life veritably began at forty, when his experimental period of constructive composition was by and he was already branching out into genuine creative effort. By this time, Clara's financial status, as a self-supporting bread winner of her household, was assured and Brahms himself was beginning to bristle with the touchy independence of the confirmed bachelor, very much inclined to have (and go) his own way. The masculine-minded youth of gentle face had merged into a sturdy, thickset being of Jove-like head,

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5In his Viennese period, when he was just the least little bit spoiled or surfeited by adulation, Brahms sometimes regretted that audiences "no longer hissed his compositions."

expansive beard and intensely masculine outside, with unsuspected sources of tenderness and gracious compassion within. Of an early picture of himself, Brahms observed: "At that time, I looked like a dubious candidate in theology." As a boy, he had virtually adopted the Schumann family and made himself a member of it. As the years go by, his manner toward Clara becomes that of a devoted son. The only differences between the two friends, as a rule, turn upon her criticisms of certain novel effects of his music, which do not square with her old fashioned sense of the fitness of things. In old age, the atmosphere about either is sometimes thunderous; effect of the ponderous pragmatism of the Nordic approach, which somehow visualizes Henry James' Italian marquis in London, waving his cane in the air and hissing: "They have *heavy* minds."[6] But it is through this unfailing high seriousness that the music of Brahms attains the heights of "splendor and magnanimity" noted by an English writer. Of impeccable structure, it has extraordinary power, not only to elevate and sustain us over the dead spaces of life, but even to exalt and ennoble. In ordinary human relations, often with Americans, Brahms was himself one of the most charming of men, and this, with all due allowance for the many anecdotes concerning his offhand bouts of old bachelor rudeness. He left one social gathering with the mocking query: "Is there anyone in this room whom I have *not* insulted?"; and a well-known silhouette represents him trudging through the streets of Vienna with an attendant hedgehog. As "there is no animal in nature so patient as the fretful porcupine," it is possible that Brahms was sometimes teased to get a "rise" out of him. Some jolly Viennese girls, who were trundling him over the ice in a little sleigh, once tipped him into a snow-bank, no doubt to hear the old bachelor curse and swear. In making a generous subscription for a prospective monument to the Swiss composer Raff, Brahms could not resist the sally: "Get that statue up quickly before the composer himself

[6]In the Princess Casamassima, à propos of the Anglo Saxon, and general Nordic talent for fumbling.

is forgotten"; and it delighted him to silence cheap flattery in the open by asserting (with uplifted forefinger) that some blatant bit of band music, then playing, was one of his own compositions. On the other hand, even his dressing table was usually cluttered up with toys to present to children on his walks; he gave his poverty-stricken father, for reference in distress, a book of religious character, which was later found to be filled with bank-notes; and to a poor waiter, bullied by a bounder, he handed a double *douceur*, whispering: "That is for the other gentleman also." In brief, a man of essentially noble nature, with occasional lapses into the sly malice of the physical dwarf (*Kleine Leute haben grosse Herzen*). Loathing adulation and all manner of lionizing, Brahms side-stepped invitations to visit England, "to make his works better known," with the dry reminder: "They are already printed for that purpose." An offer of a liberal honorarium for a new composition, "to order," was rejected with the hint that some slight attention be paid his already published works. His jeers at the trite quality of Highland reels were set off, perhaps ironically, by such "hauntings of Celtism" as his three versions of "Edward, Edward," Murray's *Ermordung*, the beautiful intermezzo on Lady Ann Bothwell's Lament (opus 117, No. 1) or his effective use of the primitive pentatonic scale of Scotland (*c, d, e, g, a*) in the andantino of the Clarinet Quintet—

> *"He's pu'd the rose o' English loons,*
> *And brok'n the harp o' Irish clowns,*
> *But our Scotch thistle will jag his thumbs,*
> *This wee, wee German Lairdie."*

Brahms' pawky humors, applied as freely to himself as to others, had, in fact, a kind of "Scotch snap" to them.

Like most men of marked originality and strong intellectual bias, Brahms was, in brief, a bundle of contrary and contradictory traits, spontaneous, whimsical and therefore unpredictable, perhaps undecipherable, even to himself. A child of the people, a patron of the folk-song, he could compose music of essentially aristocratic type, such as the violin sonatas, the intermezzo for piano or the

clarinet quintet. When the University of Breslau gave him a doctor's degree as "the master of austere music," he acknowledged the diploma on a postal card and sent in, as his inaugural dissertation, a rollicking Academic Overture on German student songs. He stood up for Beethoven's imitation of a music box in the Emperor Concerto, admired the banjo and, as the great master of polymorphic rhythms, thought even of utilizing "not the stupid tunes, but the interesting rhythmus of ragtime" (Schauffler). Did he beam with satisfaction over a new performer or a new composition, the goose of either was cooked in advance; if he looked sad and serious and sometimes left the room, he would go any length to help performer or composer. Ordinarily modest and reticent as a mouse in a corner about his own work, woe to the luckless pretender who came within range of his biting tongue! Abstemious as a miser with regard to his own creature comforts, he squandered to a fault in helping the poor and needy, supported several indigent composers or their relatives, lifted Dvorak out of obscure poverty into success, corrected his proofs and twice placed his entire fortune at his disposal. If the same whimsicality made him sometimes churlish in genteel interiors, Brahms would put himself to endless inconvenience to spare or help the forlorn and down-trodden, and actually pretended to be a Roman Catholic in Italy, out of a Quixotic consideration for a people he liked. Certain negligible eccentricities in dress and behavior he attributed to the chill penury of his boyhood, the cruel necessity which compelled a virtual child to gain his living in the haunts of vice.[7]

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[7]It is well to bear in mind that the lot of great composers in the past was not even as secure and respectable as that of hired servants today. Sebastian Bach was of less social consequence in his community than the court functionary who trimmed the toe-nails of His Serene Highness. Mozart and Haydn were virtual chattels of great personages, uniformed, like organ-grinders' monkeys, sometimes even composing music to order. Mozart, divine child of genius, fed at the servant's table, was starved by patrons, cheated by publishers, and once even kicked downstairs by an archbishop's lackey. Some of the most beautiful songs ever conceived by mortal man were composed by Schubert out of hand to pay off his beer

Up to the age of 24, Brahms had remained a beardless boy, *presqu' un éphèbe,* of seraph face and piping, high treble voice. The change to the burly, thickset, vigorous, heavily bearded man of his prime was accomplished by a corresponding change in his physiological life, which any doctor would understand, about which lengthy chapters have been published and over which any man of the world would draw a charitable veil. He pursued no neighbors' wives, daughters, sisters, cousins or aunts; indeed so unquestioned was his veneration for the married state that he terminated his lifelong friendship with Joachim, when the latter came to divorce his wife. Of a prospective *visite de noces* with a much married pianist, Brahms observed: "He is sure to marry several times again and [with kind permission] I'll just skip meeting wife No. 3." It is doubtful if Brahms' persistent backing away from the married state was anything more than the usual fugitive slave reaction of the independent artist, as in the case of Artemus Ward and the Mormon widows or of Liszt, when pursued to the very portals of the Vatican by *Fürstin Hinterlist*: "Gregory VII was a great philanthropist." In 1891, Brahms, the self-willed old bachelor, published the original version of Schumann's D minor symphony without the consent of his widow, who let loose upon him the vials of her wrath, even to a break in their oldtime

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scores in the little inn at Grinzing. Until late in the 19th Century, composer and virtuoso were regarded as performing dogs on show, who entered the house by the servant's staircase and were separated by a crosswise rope from the aristocracy. To the noble patron in an English novel, the term "musician" connotes long hair and dirty hands. Humiliations of this kind were weathered by the great composers of the past with a dignity and fortitude which are beyond all human praise. Rough handling made them rough customers, in accordance with Newton's Third Law of Motion. If today, the composer, the professional musician, have become respected and respectable, it is due to the superior social gifts of such modern men as Liszt, Chopin, Tchaikovski or St. Saens and to the upstanding independence of such dynamic personalities as Händel, Beethoven, Wagner and Brahms. For admirable research-work on the degraded status of music and musicians before the time of Wagner and of Wagner's enormous accomplishment in improving the situation, see Ernest Newman's recent life of Wagner, vol. I (New York, Knopf, 1933).

friendship. Brahms effected reconciliation by stressing his forty years of devoted service, his loneliness and the real point at issue: "Allow me to repeat that you and your husband represent the most beautiful experience in my life." Upon the strength of this simple, honest statement, we may dismiss, as idle, impertinent gossip, certain suppositions of recent biographers touching the fair fame of these two benefactors of the human race and doctored up, as usual, *ex post facto,* after the victims are dead and gone and no longer here to defend themselves. Were Brahms on hand just now, to encounter some of these prurient pickthanks, one can fancy him pouncing upon them with the agility, ability, ferocity and velocity of some of the big cats out of the tropical jungles, albeit not primarily a member of the cat family himself.[8]

The definite break in Brahms' otherwise robust health came at Clara's funeral, which he all but missed by taking the wrong train, and to which he hastened on foot in a driving rain, lingering by the grave in an extra bath of perspiration. A latent cancer of the liver was aggravated by the chill, and presently Brahms stands at the gates of death. In the virile *Totentanz* of his E minor symphony, he had greeted death in a jocund, exultant spirit. But now, his mood, as conveyed in one of his Serious Songs, is that of Odysseus in Hades: *O Tod! wie bitter bist du!.* Not only had he attained to serene satisfaction through his acknowledged position as the strongest and most dignified figure in modern German art, the last of the great line of classical composers; but latent within himself were untapped wellsprings of creative power, productive of such things as his terminal double viola quintet (opus 111), which is incandescent with genius of the highest order, incidentally a charming pendant to that radiant apotheosis of Viennese *Gemütlichkeit,* the Schubert Octet. To Brahms, in his au-

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[8]Many of the above anecdotes and data are to be found in the 8 volumes of the Life of Brahms by Max Kalbeck and "The Unknown Brahms" by Robert Schauffler. There is no well-ascertained fact about Brahms which does not go to show, what his music and the extant portraits plainly tell us, that he was an inflexibly honest and absolutely reliable man.

tumnal period, came easy mastery of the most difficult material and a magical rejuvenation, giving to his F Major Symphony or his later songs and chamber music a life-enhancing freshness and fragrance—

> *"Over the winter glaciers*
> *We see the summer glow,*
> *And through the wild-piled snow-drift,*
> *The warm rosebuds below."*

To a man so inspired and endowed, death came as a tedious, troublesome, unwelcome visitor. Toward the end, Brahms resumes the past with Georg Henschel, and what he says will convey some notion of his ideals and of what he sought to express in music:

> "How few true men there are in the world. The two Schumanns—Robert and Clara—there you have two beautiful *Menschenbilder*. Knowledge, achievement, power, worldly place—nothing can outweigh this, to be a beautiful *Menschenbild*."

No slur which may be cast upon the memory of Johannes Brahms, by microscopic or myxoscopic minds, can outweigh the splendor and magnanimity of this parting tribute to the two human beings whose friendship had meant more to him than anything else in life.

F. H. Garrison.

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HYPERPARATHYROIDISM AND ITS RELATIONSHIP TO DISEASES OF BONE*

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A brief preliminary explanation of normal parathyroid function seems necessary for the subject that follows. The parathyroids when functioning physiologically, elaborate a hormone which is secreted in such quantities as to regulate in amount and maintain within certain levels the blood calcium and possibly phosphorus. Intimately allied with the parathyroids in their process of regulation through hormone production, are such other factors as the calcium and phosphorus available in the diet, the ratio of these substances to each other, and the vitamin-D availability. These seem to be important in determining the level of physiologic activity of the parathyroid glands. Considerable evidence is accumulating to the effect that the absence of parathyroid hormone can be satisfactorily compensated for by regulation of the calcium, phosphorus, and vitamin-D intake. Tetany, following ordinary parathyroidectomy in both man and animals, can be greatly ameliorated in severity or possibly even prevented by both high calcium intakes and sufficient vitamin-D therapy.[1] Normally, then, the chief activity of the parathyroid gland is the production of a hormone that helps to equilibrate the calcium and phosphorus between the tissues and the blood.

Hyperfunction of the parathyroids, or hyperparathyroidism, but recently conceived and established, has come within the realm of actual knowledge only during the last eight years. While considerable progress has been made in the field of parathyroid hyperfunction, much still re-

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From the Laboratory Division, Hospital for Joint Diseases, New York.

mains to be elucidated. Hyperparathyroidism is now, on the one hand, synonymous with Recklinghausen's disease of bone. In this condition, a pathologic degree of hypersecretion has been proved to exist as the primary cause of the disease. Another question promptly arises here: Does hyperparathyroidism exist in other bone conditions than Recklinghausen's disease? In such diseases as rickets, osteomalacia, calcium deficiency osteoporosis, etc., where the parathyroid glands are sometimes found enlarged—is the enlargement an indication of a compensatory hyperactivity, a physiologic or secondary hyperparathyroidism? As yet, there is no definite means of proof to decide this problem.

Reverting once more to the hyperparathyroidism of pathologic degree, certain definite clinical and chemical manifestations signal the presence of parathyroid hormone secretion in abnormally great quantities. In the absence of serious complications derived from its occurrence, some of the more exact indications are: an increased serum calcium or hypercalcemia, a depressed serum phosphorus or hypophosphatemia, an elevated serum phosphatase, an increased excretion of calcium and phosphorus particularly through the urine, and—progressively, constantly—a decalcification of the bones.

Before proceeding, let us consider the general substance of this discussion. I propose to give: (1), a very brief survey of primary hyperparathyroidism or Recklinghausen's disease; (2), a review of experimental hyperparathyroidism, particularly stressing its connotations in relation to Recklinghausen's disease; (3), an examination of some other metabolic diseases of bone in their relation to Recklinghausen's disease and the possible role of hyperparathyroidism in their evolution; with, finally, (4), a discussion of the rationale and basis of the recent surgical popularity of parathyroidectomy in other bone diseases than Recklinghausen's.

First under consideration, we have Recklinghausen's disease, which has been previously indicated as the effect

of pathologic or primary hyperparathyroidism. As clinically encountered, it is usually the product of many years' more or less progressive evolution. Dependant upon the stage of its development when brought under observation, the pathologic changes in the osseous system may cover a wide range. The lesions may be so advanced as obviously to suggest the designation of generalized ostitis fibrosa cystica, or so slight as to be barely perceptible grossly. Between these two extremes are cases that evidence varying degrees and various stages of involvement. Thus, in a specific case, a long tubular bone may grossly appear entirely free of any involvement, while other long tubular bones present the more classic evidences of the disease:—marked porosity, cysts, giant-cell tumors, and an abundance of connective tissue, especially in the metaphyseal marrow cavities. Since, however, Recklinghausen's disease is a generalized one—which implies the subjection of the entire osseous system to its influence—histologic examination of the apparently uninvolved bone will, nevertheless, demonstrate microscopic indications of its presence.

Recklinghausen's disease generally evokes the image of cysts and giant-cell tumors as essential accompaniments of its pathologic features, whereas that is not necessarily so. Bones may undergo extensive resorption and transformation in the course of the malady, yet careful search will fail to disclose either gross or microscopic cysts or giant-cell tumors. Rather, the essential process due to pathologic chronic hyperparathyroidism in the evolution of the final pathologic picture is progressive demineralization; upon it, all other changes are consequent. The decalcification is the stimulus for the appearance of numerous osteoclasts with their Howship's lacunae and the proliferation of the marrow connective tissue. Finally, it is conceivable that the chronic hyperparathyroidism may incidentally, in the course of the development of bone changes, favor extensive hemorrhage into the marrow, resulting in brown blood cysts and the formation of giant-cell tumors. The pathologic picture may be modified by, and vary with,

the age of the patient, the duration of the disease, the intake and availability of mineral salts, the celerity and degree of decalcification, and stresses, strains and possible injuries to which the decalcified skeleton is subjected. As investigators are becoming more aware of the wide range of pathologic changes in the bones, produced by hyperparathyroidism, the hope draws closer to realization that the severe deformities, such as Recklinghausen originally described, by virtue of early recognition will be wholly eliminated.

The association of tumor-like, parathyroid enlargement with the bone changes of Recklinghausen's disease has become increasingly evident, especially since 1925, when Mandl made his important discovery. He was the first to recognize that immediate clinical improvement and regression of such bone changes occurs after the removal of an adenomatous, parathyroid tumor. This observation decided the question whether in Recklinghausen's disease the parathyroid abnormality was the result of the bone disease or its cause. A rapidly increasing series of cases, of which about 60 cases have since been reported, support the hypothesis that parathyroid hypersecretion is the basis for the inception of the bone lesions of generalized ostitis fibrosa cystica. In this country, further clarification of the clinical aspects of the subject was achieved principally through the work of DuBois, Barr, Boyd, Aub and their associates. In no other disease in which parathyroid enlargement has been encountered has there been like proof —as here—that there exists an actual hyperfunctioning of the parathyroid glands instigating bone changes.

The accumulated postmortem and clinical experience with Recklinghausen's disease has demonstrated variability in the number, size, weight, position, gross and histologic appearance of the offending parathyroid tissue. The examinations have shown that one or more benign, parathyroid adenomas, without any other parathyroid tissue, may be present, or an enlarged parathyroid with one or more (in some instances, four) normal-sized para-

thyroids, may be found. Thus, the likelihood of the absence of other parathyroid tissue indicates the danger of parathyroid tetany following operative removal of a benign parathyroid adenoma. As to size, the tumors have measured from 1 to 7 cm.; they have weighed as much as 35 gm. No correlation has been established between the size of the parathyroid tumor and the severity of the disease. In spite of their large size, it is amazing that so few of them have been palpated before operative removal; some of the largest glands were not palpable because they were tucked away between the esophagus and the trachea. Hypersecreting parathyroid adenomas have even been found completely within the substance of the thyroid gland, as well as in the mediastinum.

The parathyroid tumor is usually nodular and cystic; the cut surface appears yellowish; generally, where histologic semblance of normal parathyroid tissue remains, the tumor is found composed of principal cells. There have been described a few instances of fairly large parathyroid-like tumors without bone changes. It is very difficult to give any interpretation to these reports. The danger of confusing parastrumas of the thyroid with parathyroid adenomas, is only too obvious. Hereafter, in attempting to establish the parathyroid nature of such tumors, it will be necessary to prove the existence in them of the parathyroid hormone. Among the other pathologic manifestations are—metastatic calcification, particularly in the mucosa of the stomach, the lung and the kidneys; renal calculi are also commonly observed.

From the clinical standpoint, pathologic primary hyperparathyroidism is a disease but infrequently encountered in comparison with the other conditions causing extensive osseous decalcification. When such a patient does come for diagnosis, the indications and symptoms are found variable with each case. Diagnosis is often difficult to make; the clinician should consider and interpret: (a) the history and physical examination, (b) the chemical analyses and radiographs—always relating them to the

history and physical examination; finally, (c) he must consider differentially the other conditions that lead to decalcification and porosity of the bones and which may simulate Recklinghausen's disease. It is not my purpose here to discuss in detail the means of arriving at a diagnosis. This has been done in the many excellent clinical articles published. Suffice it for the purpose of this presentation to differentiate Recklinghausen's disease from certain others by reference to its more precisely individual characteristics.

We come now to the second consideration of this discourse:—a review of experimental hyperparathyroidism, with especial emphasis on its relation to clinical Recklinghausen's disease. With Collip's preparation of the active parathyroid extract, it has been possible to study hyperparathyroidism in the experimental state. In association with my colleagues, Doctors Bodansky and Blair, certain of its effects on animals have been demonstrated. Repeated, small, nontoxic doses of this extract, injected into dogs, soon raises the serum calcium and causes an increased excretion of calcium and phosphorus through the urine. The dog is so particularly sensitive to moderate dosage, as well as to overdosage, that unless the calcium intake of the animal is restricted or the dosage of parathyroid very limited, fatal toxic effects with marked hypercalcemia and hyperphosphatemia are likely to ensue. Dogs on either a liberal or low calcium intake, when treated for some time with parathyroid extract, show a regression of the initial tendency to hypercalcemia. On a low calcium intake, the regressing hypercalcemia may eventually be replaced by a hypocalcemia. Sometimes, such dogs die from the toxic effects of the parathyroid extract, without even evincing a terminal hypercalcemia. In dogs, with chronic experimental hyperparathyroidism, the serum phosphorus tends to remain at or to exceed the normal level, regardless of whether the calcium in the diet has been low or liberal. This hyperphosphatemia contrasts with the hypophosphatemia usually observed in clinical cases of

Recklinghausen's disease without nephritic complication. This, of itself, indicates the great sensitivity of the dog to injections of parathyroid extract.

On either the adequate or low calcium diet, the dogs with experimental hyperparathyroidism demonstrate bone decalcification and resorption, and reactive marrow fibrosis. These are also the basic histologic changes observed in the bones of clinical cases of Recklinghausen's disease. We have been led to conclude from our experiments that the dog has a much greater sensitivity to hyperparathyroidism than man. Whether the difference in their reactions is more apparent than actual, one cannot say. In the course of Recklinghausen's disease in man, much more delicate adjustments and compensations are probably made than in the dog.

However, other animals, by reason of their greater resistance to parathyroid extract, open other aspects of the problem. In the rabbit, the effects of parathormone, if elicited at all, are very slight. Hypercalcemia can be evoked by a single dose only when it is extremely large; toxicity, or overdosage effects as seen in dogs, is absent in rabbits given repeated, large, daily doses, when preliminary treatment with smaller doses has been administered. Furthermore, the injection of as much as 4,200 units, into a young adult rabbit, during 90 days of treatment, led to practically no bone changes.

The guinea pig, although relatively resistant, is much less so than the rabbit. It is possible to obtain in young guinea pigs, early in the course of repeated daily treatment with parathormone, hypercalcemia and hyperphosphatemia, decalcification and fibrous transformation of rapidly growing bones or portions of such bones. In young and adult guinea pigs, a compensation is established during prolonged treatment, which enables them to tolerate repeated, large doses, without hypercalcemia, and which permits considerable repair of bone lesions produced earlier in the treatment. Healing of the bone lesions in the guinea pig brings about a definite progression towards normal bone.

On the other hand, the rat, as we will presently see, has an altogether different healing response. The rat, whose bones are fairly reactive to parathormone, unlike the dog, tolerates relatively large doses without too great a risk of fatal hypercalcemia and hyperphosphatemia. Therefore, the rat can be given a high or adequate calcium diet, when injected with parathyroid extract. After short periods of treatment with relatively large doses, the bones of rats manifest all the usual changes of hyperparathyroidism:—pronounced decalcification and resorption, and the appearance of fiber marrow. However, it is notable that rats fed an adequate calcium diet and kept on parathyroid extract for long periods of time finally evidence the development of marked cortical thickening, and metaphyseal osteosclerosis. This osteosclerosis is to be interpreted as a superabundant healing phenomenon. The bone thickens because new-bone formation is excessive, but it occurs in the presence of continued bone resorption. Such rats are apparently in calcium equilibrium in spite of long treatment with parathyroid extract; this is one of the reasons for the peculiar healing response. The microscopic appearance of such sclerotic bone simulates, but does not exactly duplicate Paget's bone. The suggestion in that direction springs from the numerous cement lines somewhat chaotically disposed. This osteosclerosis reflects the mechanism of construction of sclerotic bone as seen in Paget's disease, or possibly Albers-Schoenberg's disease, although the etiologic circumstances are seemingly entirely different.

In our experimental studies of hyperparathyroidism, the mechanism by which bone decalcification and resorption are brought about, has always been of particular interest to us. The histologic study of a great number of decalcified and undecalcified bones, from animals suffering from experimental hyperparathyroidism, has led us to the conclusion that hyperparathyroidism (as a result of the changes that it induces in the tissue fluids circulating about the bone) has but one primary effect: That is, the solution of mineral salts out of the bone. This halisteresis

occurs at the surfaces of contact between the tissue fluid and the bone. All other appearances and effects are secondary to the production of minute and narrow zones of decalcification on the subperiosteal, subendosteal, trabecular and Haversian canal surfaces.

We thus come to the logical question: what has the animal experimentation taught us in relation to clinical Recklinghausen's disease? We should first recognize that complete duplication of the advanced form of this disease as seen in man is not practicable in animals, because of inherent limitations. The difficulty resides in the variable, but native, tendency of animals to compensate against the induction of experimental hyperparathyroidism, although never immunized to the extract. Despite this, and provided suitable animals and dosage are employed, it is possible with parathyroid extract to produce hypercalcemia, increased excretion of calcium and phosphorus through the urine, bone decalcification, the appearance of osteoclasts in Howship's lacunae in the course of the resorption, and fiber marrow. Whether the commercial parathyroid extract used in these experiments is actually the unchanged hormone of the parathyroid gland, one cannot say. Nor, again, can one determine at this time, the possible difference of this extract from the hormone elaborated by a hypersecreting parathyroid adenomatous tumor. The existence in man of a state of perverted mineral metabolism, as a prerequisite for the disease, appears to be excluded, as removal of the hypersecreting parathyroid adenoma alone apparently allows complete reversal of the pathologic state.

This brings us to the third division of our subject: the examination of some other diseases of bone in their relation to Recklinghausen's disease and the possible role of hyperparathyroidism in their evolution. The condition with which Recklinghausen's disease had most often been confused is genuine osteomalacia. There is no longer any real reason for these to be so mistaken. Anatomically, the bones in osteomalacia show very little marrow scarring, rela-

tively few osteoclasts, wide osteoid margins, and the absence of typical giant-cell tumors and cysts. Chemical analyses usually show—in contrast with Recklinghausen's disease—marked reduction in serum calcium and a negative balance for calcium, but the loss is chiefly through the stool. Furthermore, while the condition of the parathyroid glands may be completely normal in osteomalacia (which is never the case in Recklinghausen's disease), occasionally slight enlargement of all four parathyroids may be encountered, while even more infrequently one of these glands may reach a fairly large size. Erdheim indicated that even when the parathyroids are not grossly enlarged, microscopic evidences of hyperplasia may exist.

The distinction between Paget's disease and Recklinghausen's disease has been made very clear in recent years. The participation of the periosteum in the production of the pathologic lesions of Paget's disease is in contrast to the lack of periosteal activity in Recklinghausen's disease. Lamellation and thickening of the cortex of long tubular bones of the type seen in florid cases of Paget's disease do not occur in Recklinghausen's disease, in which the cortex is thinned. Giant-cell tumors of the nature of Recklinghausen's disease do not occur in Paget's disease. Microscopically, the bone transformed by Paget's disease shows the rather characteristic mosaic architecture. The parathyroid glands lack the tumorous enlargement that is seen in Recklinghausen's disease, and if there is any enlargement, it is but slight and generalized. The clinical examinations of the blood have shown no particular abnormalities in Paget's disease, except that the serum phosphatase tends to be very high, in fact, higher than in most other diseases of bone. Furthermore, studies of mineral balance have given no constant results in Paget's disease, while in Recklinghausen's disease there is a constant loss of calcium.

Generalized osteoporosis is an exceedingly common condition in adults. Vitamin deficiencies, endocrine disturbances, mineral dietary deficiencies, any one of a great number of causes may be responsible for the appearance of

marked demineralization. Very often, the underlying cause for the osteoporosis is so evident that no confusion whatever arises with Recklinghausen's disease. In senile osteoporosis, pronounced rarefaction of the skeleton may occur. Roentgenographic study of the bones, especially where the spine is deeply involved, may be misleading in the direction of Recklinghausen's disease. The pure microscopic lesion of senile osteoporosis is simply a chronic fatty atrophy of the bone. In an occasional and very advanced case of senile osteoporosis, small, single and confluent cysts—oily cysts due to liquefaction of fatty marrow—may be observed in some of the long tubular bones. In addition, more or less large brown areas containing hemosiderin but without giant-cells are occasionally seen and are referable to recent hemorrhage. The parathyroid glands, when studied, are often found to be normal; they have occasionally been reported showing enlargement recognized by the naked eye. Aside from the clinical suggestions, senile osteoporosis is not in the least related to Recklinghausen's disease and can be easily differentiated when it is considered in arriving at a diagnosis.

Furthermore, not all cases with generalized fibrocystic lesions of bone are necessarily Recklinghausen's disease. Unless such cases show the clinical and chemical evidences of Recklinghausen's disease, they are still to be included in the group for which the basis is as yet uncertain.

The parathyroids may or may not be enlarged in the conditions noted before. In other conditions, as clinical and experimental rickets, multiple myeloma, extensive carcinomatous metastases to the skeleton, the parathyroid glands likewise may or may not show enlargement. If parathyroid enlargement is present in any of the enumerated diseases, it does not appear, as in Recklinghausen's disease, in the form of a benign tumorous new growth. If encountered, one or as many as all four glands may be increased in size and weight. They are rarely, if ever, more than two or three times normal size. To establish hyperplasia of the parathyroids in any of these disturbances,

measurement of the size must be supplemented by proper histologic examination: this only can determine evidence of hyperplasia and unless it is adduced, hyperactivity of the glands, a priori, must be ruled out. It is often necessary to make serial sections of the parathyroid to demonstrate hyperplasia, and of even greater value is the staining of these sections for intracellular lipoid. Hyperplastic chief or principal cells show a lack or absence of intracellular lipoid.

Assuming that parathyroid hyperplasia is established in any such case, its place in the disease evolution is still indeterminate. Does this hyperplasia connote a hypersecretion, i.e., hyperparathyroidism? It may or it may not: if it does, the increased secretion of parathyroid hormone is secondary to the bone lesions or the disturbed state of mineral metabolism, and probably beneficial, rather than deleterious as it is in Recklinghausen's disease. Accepting the parathyroid enlargement in these conditions as associated with a hypersecretion, we have no way of proving such a state, as the only exact criteria for judging hyperparathyroidism are based on the pathologic effects of hypersecretion of the hormone. Functional or physiologic hyperparathyroidism can not as yet be measured. The very fact that the parathyroid hormone takes an important part in calcium metabolism in the normal person suggests that a disease causing a disturbance of mineral metabolism may secondarily provoke parathyroid hyperplasia and thereby hypersecretion. This may be interpreted as part of the attempt at adjustment or compensation to better control the mineral metabolism. Furthermore, subsidence of the original factors producing the parathyroid hyperplasia has, in certain proved instances, been associated with return of the parathyroids to normal size.

Now, the question of the rationale and basis of recent surgical popularity of parathyroidectomy in other diseases than Recklinghausen's is to be examined. This has been practiced especially in a group of conditions which

have been described under the title of "ankylosing polyarthritis". Reviewing some of the surgical literature that discusses this problem, one is struck by the multiform and often basically different conditions that are encompassed by this term. Included are instances of the Bechterew or Marie-Strumpell spine. This form of ankylosing spondyloarthritis may, of course, also be associated with stiffening of some of the larger joints—for instance, hips and shoulders. Then again, examples of the purely degenerative spondylosis deformans with osteophytic lipping and ankylosis of the vertebral bodies are also included under this vague title of "ankylosing polyarthritis", as are instances of hypertrophic arthritis and arthritis deformans tending toward or showing ankylosis.

The evidence that a so-called "parathyroidism" exists in these conditions, which can be corrected by removal of one or two parathyroid glands, rests on very tenuous testimony. They are: first, the raised serum calcium that is frequently reported found in "ankylosing polyarthritis" —the hypercalcemia reported as subsiding after parathyroidectomy; secondly, that these patients have enlarged parathyroid glands; and thirdly, that such patients are rapidly improved following parathyroidectomy. Critical examination of this data shows that the highest incidence of hypercalcemia has been reported from European clinics. The danger of obtaining misleading calcium values on technical grounds cannot be too greatly stressed. In this country, those who subscribe to the "parathyroidism" view for "ankylosing polyarthritis" have generally found normal calcium figures, but stressed the need of repeated examinations. Furthermore, if one accepts the results of Bauer as valid—and his work has surely been done under the most favorable auspices—then neither hypercalcemia nor disturbances in mineral balance occur in "ankylosing polyarthritis." Secondly, those who favor parathyroidectomy in "ankylosing polyarthritis", state that the removed parathyroids are enlarged and hyperplastic. Now, if one examines their published photographs, it is plainly evident

that the glands architecturally appear entirely normal—there is no evidence of adenomatous hypertrophy. Besides, they have failed to seek the more accurate indications of hyperplasia by staining for intracellular lipoid. Thirdly, the reason for the clinical improvement in such patients may be entirely unrelated to the parathyroidectomy. In a number of instances, where improvement has been reported following operative intervention, histologic examination has failed to disclose the presence of parathyroid tissue in the specimens removed. Besides, even when, as by Oppel, one complete thyroid lobe was removed, to insure partial parathyroidectomy, no improvement occurred in 16 of the 49 cases. It seems that any immediate improvement that does occur is possibly associated with rest in bed, and any permanent improvement to a remission or spontaneous subsidence through regression of the activity of the process. This generalization would seem to prevail against the value of parathyroidectomy in Paget's disease as well.

Parathyroid removal is, then, only clearly warranted in Recklinghausen's disease where a benign, tumorous adenoma exists.

METABOLIC DISTURBANCES IN RELATION TO THE TEETH*†

CHARLES F. BÖDECKER, D.D.S.

INTRODUCTION

The principal purpose of this paper is to call the attention of the medical profession to its responsibility in preventing dental disorders. Recent investigations indicate that dental health may sometimes be linked with general health, and that dental ailments may be symptoms of systemic derangements. Hence it is necessary that physicians in general and pediatricians in particular should evince more interest in dental problems.

General practitioners of medicine and dentistry who attempt to cover their vast fields are interested mainly in generalities; it is therefore the aim of the author to confine himself to these, and to leave the details for the study of those particularly interested in this subject (pediatricians and dentists). For these a fairly extensive bibliography is appended.

The teeth have been regarded until very recently as organs outside of the field of nutrition. As a result of such an erroneous conception, the field of dentistry has long been relegated to a group of specially trained men who combat the diseases of the teeth merely by reparative means. The only preventive treatment instituted to protect the dental mechanism against destruction has been an attempt to promote oral cleanliness. If such cleanliness is defined as a sterility of the oral cavity, then it can be regarded as futile.

The present form of dental service, inadequate as it is in really *preventing* dental destruction, is available to only a small part of the public. The proportion of the popula-

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* From the laboratory of Histo-pathology, Columbia University School of Dental and Oral Surgery, New York.

† Delivered November 3, 1933.

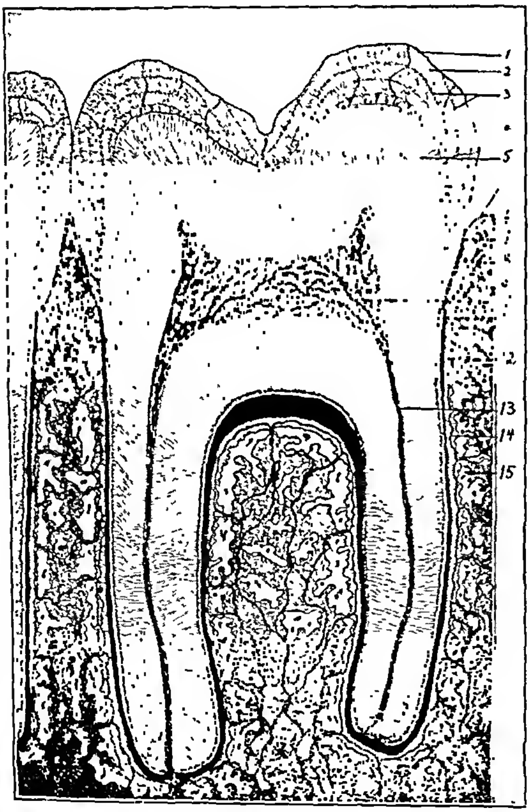
tion who receive dental care has been variously estimated to be no higher than twenty to thirty per cent. The reason why only symptomatic treatment has been resorted to by the dental profession as a whole is that systemic disturbances were thought to have no ill effect on fully formed teeth. It was believed and is still considered by many to be true that the calcified dental tissues receive no "nutrition" (added mineral salts), hence a disturbance of the nutritional balance of the body could have no ill effect on the teeth. Such erroneous views are very slowly giving way to a more sane, a more biological conception of the dental organs. Some health workers in general and the promoters of food products in particular, have filled the columns of periodicals and journals with commands to "feed your teeth." However praiseworthy this may be, a great deal of investigation must be undertaken before such an act can be understood scientifically, and furthermore, much work must be done to define the specific beneficial elements necessary to dental health. We know as yet too little of the histo-pathology of the dental tissues and almost nothing of their physiological activity. Dental physiology, as applied to the metabolism of the dental tissues, is in fact an almost non-existent science. With this in mind it is comprehensible that, as yet, little definite information can be given as to the relation of specific systemic disturbances to dental diseases.

Tissues of the Teeth

Some knowledge of the dental tissues is necessary for the comprehension of the manner in which metabolic disturbances may affect the teeth. A diagram, Figure 1, shows a longitudinal mesio-distal section of a lower molar and surrounding tissues. It is noted that the dentin forms the bulk of both the crown and the root of the tooth. Its formative and probably its nutritional organ, the dental pulp, or "nerve", occupies the interior of the crown and root; it is profusely supplied with blood vessels and nerves. The root dentin is covered with cementum which serves for the attachment of the root to the surrounding bone,

while the crown dentin is protected by enamel of varying thickness to withstand the force of mastication. It will be seen that each tooth can be regarded as a functioning unit, having its biological connection with the body through the vessels and nerves of the dental pulp. Incomprehensible as it may seem from a biological point of view, the dental pulp is believed by most investigators to have no function (except to form secondary dentin) after the completion of the tooth. In spite of the presence of a

Fig. 1. A Mesio-Distal Section of a Lower Molar, Alveolus and Gingival Papillae.*



1. Position of enamel cuticle.
2. Enamel rods showing gnarled character.
3. Striae of Retzius, incremental lines on enamel.
4. Dentino-enamel junction.
5. Tubules in the dentin.
6. Epidermis.
7. Old idea of gingival crevice.
8. Dermis of the gingiva.
9. Blood supply.
10. Dental pulp with profuse blood supply.
11. Granular layer of Tomes, situated only in the root, covered by cementum.
12. Cementum, thinnest at the cervix; thickest at the bifurcation and apices of the roots (solid black).
13. Pulp canal.
14. Peridental membrane attaching the root of the tooth (cementum) to the surrounding alveolar bone.
15. Lamina dura of the alveolus frequently perforated for the passage of blood vessels to supply the peridental membrane.

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* From Charles F. Bödecker, "Elementary Histology for Dental Hygienists." New York, 1933. John Felsberg, Inc.

profuse blood and nerve supply in the dental pulp, it is believed that the calcified dental tissues, particularly the enamel, have no connection with the body. This erroneous view seems to be held by all except Beust[1], Fish[10], and the author[2,3]. The newer researches, however, are forcing more and more investigators to accept a saner biological conception.

An examination of Figure 1 shows that the enamel, covering the entire exposed portion of the tooth, is a protective tissue to prevent destruction from the outside. The resistance of the tooth, particularly of a young person, is therefore primarily dependent upon the ability of the enamel to withstand attack of the acid which is supposed to be active in dental caries. Evidence is accumulating to show that the resistance of the enamel (and also that of the dentin) against external attack is dependent upon systemic conditions. When this is finally proven, the varying activity of dental caries will become more clear. The entire subject is now under active investigation by the Columbia University Dental Caries Research Group, financially assisted since 1930 by the Commonwealth Fund of New York.*

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* The Commonwealth Fund Grant for the Study of the Cause of Dental Caries:

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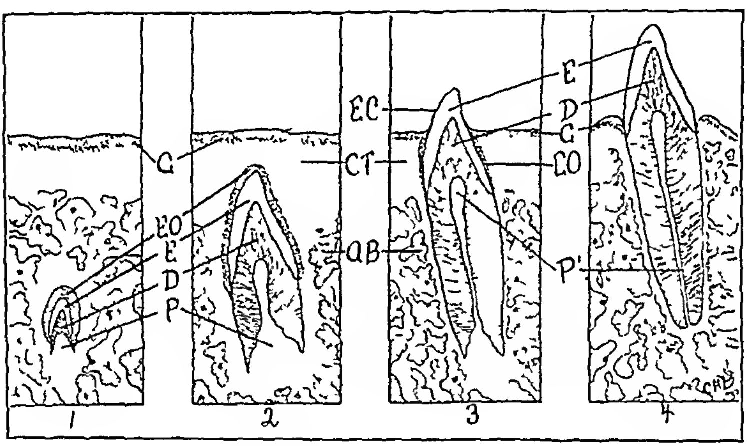
Mention must be made of the manner in which the teeth are developed; for the proper understanding of the metabolism of the dental tissues. A comprehension of the development of the enamel is particularly essential in this respect. This structure is formed by the enamel organ of ectodermal origin. Enamel growth of the teeth begins at the dentino-enamel junction and progresses outwardly, so that the last formed enamel is on the surface of the tooth (Figure 2, diagrams 1 and 2E.) The tooth then

Fig. 2. Stages in the Eruption of a Tooth.



The enamel organ is destroyed when the tooth pierces the gingiva, hence it is believed that the enamel requires no further mineral salts.

G—Gingiva.	D—Dentin.	EC—Enamel Cuticle.
EO—Enamel Organ.	P—Pulp.	CT—Connective Tissue.
E—Enamel.	P_1—Dental Papilla	AB—Alveolar Bone.

pierces the gum tissue in order to become a functioning unit of the oral cavity and thus the enamel organ is destroyed. (Figure 2, diagrams 3 and 4.) Its remnant forms the enamel cuticle (EC) which, being cut off from all blood supply, can no longer function; thus no new enamel can be developed after the eruption of the tooth. *It is for this reason* that the mistaken conviction has so

long existed that systemic disturbances cannot affect the enamel by means of the circulatory system and that therefore fully formed teeth can be acted upon only from the exterior; *i.e.,* by the saliva, bacteria, and by food retention in the oral cavity. This belief has long been a barrier to the investigation of the possible systemic causes of dental caries.

A further strengthening of this erroneous belief was the conviction that this tissue is a purely mineral structure, containing no protein matrix. If this were true, then it would be impossible for lymph, originating from the dental pulp, to penetrate the enamel. As has been stated previously, the young functioning tooth was considered to be completely matured and no mineral salts ("nutrition") were needed after this time. The comprehension of the attitude of most investigators of teeth is necessary for a thorough understanding of the problem of dental caries. Hence it is essential to recapitulate the incorrect conception of the enamel held by many investigators even today; this is that the enamel of fully formed teeth can not be affected from within by general metabolic disturbances because:

a. Its formative organ is destroyed on the eruption of the tooth.

b. It is an inorganic structure, containing no protein matter which might serve as channels for the distribution of mineral salts.

c. It is therefore impermeable to a possible calcifying or decalcifying lymph which might originate from the blood stream by way of the dental pulp and the dentin.

For these reasons, the enamel was considered to be completely matured when the tooth pierced the gum, and therefore systemic disturbances, whatever their nature, could not affect the "nutrition" of the enamel. In line with this reasoning, it was thought that a deleterious influence could affect the enamel only from the exterior.

This view is slowly losing ground as:

a. The enamel has been shown to contain a protein matrix, which may include channels for the transportation of lymph; this matrix is more abundant in youth than in later adult life. [Bödecker[3], Gies[4], Malleson[5], Bibby[6].]

b. The enamel, under certain conditions, has been shown to be permeable to dyes, etc., in vitro and in vivo. [Bunting and Rickert[7], Beust[8], Klein and Amberson[9], Fish[10], Bödecker[11,12], Applebaum[13,14].]

c. The enamel has been shown to undergo a progressive hardening after the eruption of the teeth. [Karlström[15].]

d. The enamel shows structural variations in calcification as defined by the Grenz-ray (soft x-ray). [Hollander, Applebaum and Bödecker[16].]

All these observations support the view that the enamel is permeated, at least in children and young adults, by a lymph which may increase its hardness, and protect it against the external destructive products of bacteria and decomposing food debris. It is possible therefore that dental caries, which is most prevalent in children and young adults, may be due to a failure on the part of the body to mature the teeth thoroughly after their eruption and to build up sufficiently their resistance to external attack.

The irritating cause of dental caries is probably an acid, formed by the decomposition of food debris around the teeth; this we term the *environmental* (exciting) cause of caries. This factor, however, does not complete the picture of the disease; a predisposing factor seems also to be present.

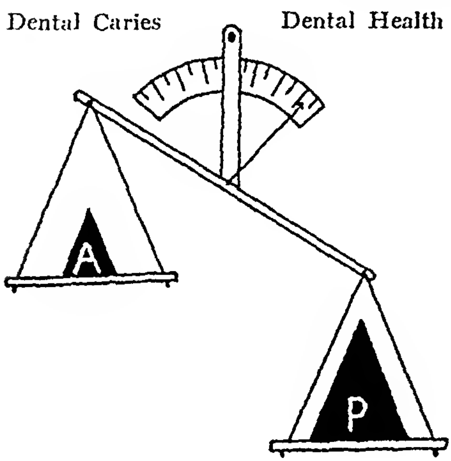
Balanced against the environmental causes of dental caries, there appears to be a *protective* mechanism in each tooth (the dental pulp), which increases the resistance of the dental tissues to attack. Figure 3 a, b, c, expresses the

Fig. 3. Diagrams to illustrate the two opposing factors active in dental caries. The exciting cause of the disease is the fermentation of food debris and other factors affecting the teeth from the *exterior*. This is shown in the diagrams as the attacking factor (A). Opposed to this is the protective factor (P), a defense mechanism active from the *interior* of the tooth; its activity is dependent on systemic conditions.

Fig. 3a.

HIGH IMMUNITY TO DENTAL CARIES

(Primitive Races)



DENTAL ATTACKING FACTOR

(A)

Weak: due to natural diet and intense use of teeth; oral prophylaxis unnecessary.

DENTAL PROTECTIVE FACTOR

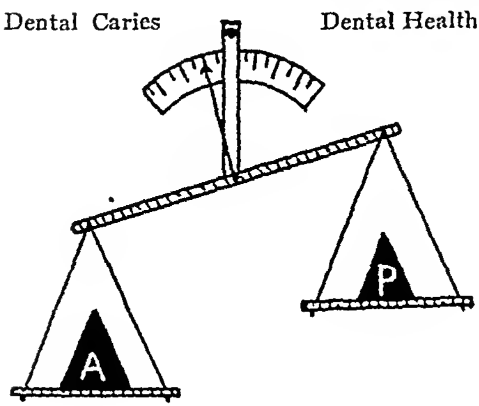
(P)

Strong: due to good general health.

Fig. 3b.

SLIGHT SUSCEPTIBILITY TO DENTAL CARIES

(Average Civilized Persons)



DENTAL ATTACKING FACTOR

(A)

Strong: due to adhesive civilized diet resulting in considerable food retention; oral prophylaxis brings dental caries to a standstill.

DENTAL PROTECTIVE FACTOR

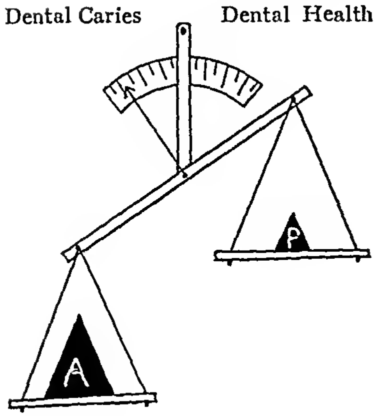
(P)

Weak: due to a reduction of vitality of the body (unbalanced diet, lack of sunshine and exercise).

Fig. 3c.

GREAT SUSCEPTIBILITY TO DENTAL CARIES

(Persons suffering from systemic disturbances)



Dental Attacking Factor

(A)

Very strong: due to excessive food retention resulting from disuse of painful teeth; oral prophylaxis useless, due to weak dental protective factor.

Dental Protective Factor

(P)

Very weak: due to metabolic disturbances.

view of the author concerning the mutual relationship of these two major factors active in dental caries. The proper functioning of the protective mechanism is dependent largely on optimal systemic conditions. It is therefore clear that the attacking factor (food debris, bacteria, etc.) is counterbalanced by the protective factor. Thus a reduction of the natural protection of the teeth, through systemic disturbances, results in an increased activity of dental caries, unless it is counterbalanced by a more strict oral hygiene; frequent use of the tooth brush removes the food debris around the teeth and thus reduces the formation of oral acid (Figure 3b).

Civilization has changed our diet as well as our habits, so that our physical resistance has been lowered, in comparison to that of primitive people. Thus the teeth have lost their natural protection and we must resort to artificial means of cleansing to reduce the environmental causes of caries (food debris, bacteria, etc.), in order to combat dental destruction. This brief description of the two opposing factors of dental caries explains the necessity for scrupulous oral hygiene in *civilized* people, for most of us have a lowered resistance to dental caries.

Persons with rampant caries (Figure 3c) have such an exceedingly low resistance (P) that no amount of brushing of the teeth can prevent their decay.

Fig. 4. X-ray of two central incisor teeth which shows that saliva, food retention, and bacteria cannot be the only factors in the cause of dental caries, as only one of the two closely adjoining tooth surfaces has become carious.

The findings of the Agnews[17], Boyd and Drain[18], Eddy[19], Percy Howe[20,21], Hanke[22], Martha Jones[23], Marshall[24,25], McBeath[26], Klein and McCollum[27,28], May Mellanby[29,30,31], Price[32,33,34], and others show that dental disorders may be greatly reduced by a proper adjustment of the diet. Some of these investigators maintain that a lack of vitamin C is principally responsible for the activity of dental caries (Howe, Hanke). Weston Price regards vitamin B and mineral salts as the important elements in a caries free diet. Some believe that the lack of vitamin D is the offending factor (Mellanby). Finally, a disturbance in the calcium-phosphorus balance (which includes vitamin D) is the factor to which most recent investigators point as being

responsible for the high activity of dental caries. This conception is held by the Agnews, Jones, Marshall, Klein and McCollum, as well as by the Columbia University Dental Caries Research Group. The report of this group to the Commonwealth Fund, March, 1933, contains among much other material this statement:

"It is clear from these experiments that systemic factors associated in some way with the calcium-phosphorus metabolism are definitely related to the resistance of the teeth to decay. Whether other systemic factors exert an influence remains for future investigations to determine."

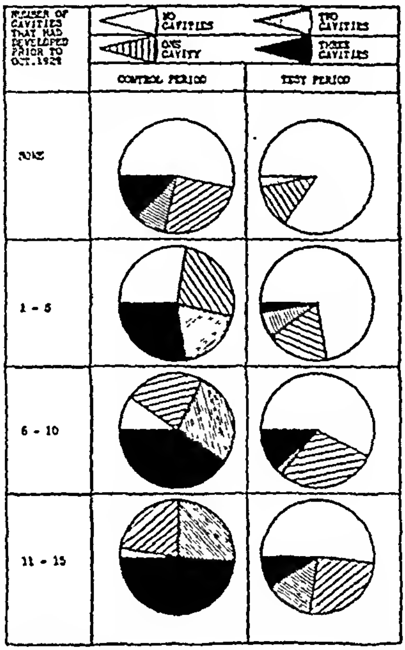
The sources of vitamin D appear to be an important factor in the prevention of dental caries, as shown by the observations of McBeath, of our group. This investigator was able to reduce dental caries to one-ninth its activity by irradiating children, ranging in age from 8 to 14 years, with ultra-violet light; that is, *dental caries was nine times more active in the control group than in the experimental group.* Mellanby and Jones believe that a diet, composed largely of cereals, is harmful, inasmuch as they have observed a marked increase of dental caries under these conditions. Hanke (Chicago Dental Research Club) has recently published an extensive report concerning "Nutritional Studies on Children[22]." Their results are typical of the work of other investigators in reducing dental caries by dietary means. Observations were made on 323 children over a period of two years; the results are shown in a copy of one of their graphs (Figure 5).

Discussion

The foregoing brief report of experiments to control dental caries by dietary means shows that it is possible, in the majority of children, to reduce and even in certain cases to prevent, this very common destructive dental disease. The divergence of opinion, concerning the specific beneficial factors, active in maintaining dental health indicate that our problem is not yet solved. Furthermore, the harmful elements of the diet which seem to exist, have

Fig. 5.

Correlation of the number of cavities that had developed to October, 1929 (total previous decay) with the incidence of dental caries during the control and test periods.



Each circle is divided into segments which show the percentage of children in which no, one, two and three (or more) cavities developed during the period designated above. The number of cavities that had developed prior to October, 1929, appears at the left. Read circles from left to right to determine changes occasioned by a change in diet. Read circles from top to bottom to determine variations in the incidence of dental caries associated with an increasing tendency toward this disease.

From "Nutritional Studies on Children," M. T. Hanke, et al, The Chicago Dental Research Club, *Dental Cosmos* 75, 742, August, 1933.

not yet been definitely specified. An excess of carbohydrates is still held by some investigators to be partly responsible for an increased activity of dental caries. The work of Mellanby and Jones indicts cereals as the principal cause of the great activity of dental caries. Cereals have been fed commonly to generations of children, and it is possible that this type of diet, which forms an acid ash in the body, is harmful to the teeth and explains at least in part the intense activity of dental caries in the young [Mellanby[30], Jones[23] and Kugelmass, King and Bödecker[35]]. Kugelmass expresses a definite opinion on this subject: "children maintained on ketogenic diets, *base-forming* in

their mineral content, showed low life caries indices, while those maintained on ketogenic diets, *acid-forming* in their mineral content showed marked dental caries." Further that: "children free from dental caries showed consistently a dietary intake excessive in alkali-forming minerals, with a preponderance of raw fruits and vegetables."

The following quotation of Hanke[22] is interesting inasmuch as it indirectly throws light on the relation of the teeth to the body. Hanke says: "It is becoming increasingly evident that dental caries can be influenced in some cases by modifying the diet. The change in diet must, then, either lead to a change in the oral condition or lead to a change in the tooth itself. It is impossible at present to determine just why dental caries should be arrested by a change in diet. An incontrovertible proof as to whether the change occurs in the oral cavity or in the tooth itself is not contained in our studies nor in those of other investigators to which we have had access."

The results of McBeath[26] are particularly instructive in this respect, inasmuch as the beneficial effect of ultra-violet light rays does not reach the teeth by way of the mouth, but must affect primarily the systemic condition, which in turn improves the resistance of the dental tissues to caries. All forms of dietary additions such as orange juice, cod liver oil, vegetables, fruits, etc. come into direct contact with the teeth and therefore might be thought to increase their resistance to dental caries by means of this contact. But this condition does not apply to the observations of McBeath concerning the effect of ultra-violet light. It is thought by many investigators that the saliva is the beneficial or harmful agent affecting the teeth during varying systemic conditions, but Figure 4 shows that this can not always be true. In this x-ray we note that caries has attacked only one of two closely adjoining teeth. Saliva can not be made responsible for attacking one tooth and protecting the other.

The fact therefore that teeth may be benefitted by ultra-violet irradiation is an indication of their biological con-

nection with and dependence upon the body. The frequent reiteration of this statement may seem needless to an audience composed principally of biologically-minded medical practitioners, nevertheless it is necessary, in order to break down the prejudice under which most investigations of dental caries have been carried on.

A study of the recent literature on the subject of dental caries shows marked contradictions. Some investigators point to the advantages of a diet composed chiefly of fruits and vegetables and stress the benefits of ultra-violet light. They strengthen their argument with examples of the excellent teeth noted in some primitive races living in the tropics. Contradictory evidence in this respect is presented by the Eskimos, who live six mouths in darkness and subsist on an entirely different diet, a high protein diet. Their teeth are in an excellent condition so long as the race is not exposed to our civilized diet [Waugh[36]]. These two contradictory observations are so confusing that some people have disregarded diet as a major factor in the cause of dental caries. However, Martha Jones suggests a rather ingenious explanation of this paradox. She believes that an abundance of ultra-violet light, such as people of the tropics enjoy, results in a slight acidosis, hence such people require a highly alkaline diet, namely fruits and vegetables to maintain the normal balance. The Eskimos, on the other hand, living in a region where there is a scarcity of ultra-violet light, tend as a result to an alkalosis; hence they require a higher acid ash diet in order to counteract this alkalosis. This view appears plausible, for it is a common practice of dietitians to advise the reduction of meat consumption during the summer months in the temperate zones, and the increase of the protein content of our diet during the winter months. Dr. Jones is continuing her researches in this direction and if her views are correct, it will clear our conception of the type of food necessary to maintain dental health under different climatic conditions; and thus the apparent paradox of dentally perfect races living on radically different diets will be removed.

Dental caries is undoubtedly due to a number of causes. The author suggests that the relation of the teeth to systemic disturbances may be expressed tentatively in the diagram shown in Figure 6. This chart is presented merely to crystallize our thoughts on the problem. If this theory, showing the complexity of the causes of dental caries is approximately correct, we begin to understand why the views of different investigators are so widely divergent, and to comprehend that each may be correct in his individual observations made in localized districts. For instance, the activity of dental caries in one locality may be due to a lack of sufficient mineral salts resulting from an impoverished soil, as is claimed to be the case in South Africa. [Lennox[37]] In a second locality, dental caries may be caused by a lack of sufficient sunshine; in a third, to an absence of one of the vitamins. Naturally each observer believes that the deficiency he observes is the sole cause of dental caries; and he may be correct so far as his locality is concerned. The chart (Figure 6) shows a number of deficiencies, each of which may be regarded as a contributing factor in dental caries, since such a deficiency can disturb the metabolism of the body. This in turn reacts on the dental pulp, the nutritional organ of the tooth. A disturbance of the function of this organ results in a derangement of the protective mechanism of the tooth; this constitutes the predisposing cause of dental caries. It is only when the natural protection of the teeth is lowered through an improper functioning of the dental pulp that the exciting causes of dental caries can become active (food debris, bacteria).

All investigators who have observed nutritional experiments have noted that the activity of dental caries is reduced under improved nutrition. But the fact that this disease can not be prevented in all cases, again shows that our understanding of the problem is by no means complete. We do not yet comprehend the mechanism of destruction of the dental tissues during the feeding of an unbalanced

diet; neither can the manner be agreed upon in which the teeth are protected during the period of proper nutrition. This protective dental mechanism whose disfunction allows the teeth to be ravaged by dental caries, must first be defined by the histologist and physiologist in order to make further progress in the solution of the problem of dental caries. When that is achieved, attempts will be made by the chemists to analyze the dental lymph and to find differences in the constitution of this fluid in caries-immune and in caries-susceptible persons. Then, knowing the elements necessary to maintain a high resistance of the teeth to decay, we may possibly administer these elements to the body, at the same time stimulating the organs responsible for their assimilation. It will be important also to define those food elements affecting body fluids which result in systemic disturbances permitting the decalcification of the teeth; when these are recognized, the medical profession can warn the public of the dangers of an improper diet, and can stimulate public interest in individual responsibility in maintaining general health for the possession of sound teeth.

Conclusion

Recent findings indicate that a disturbance of the calcium-phosphorus balance exerts a deleterious influence on the teeth, making them more prone to dental caries. In the light of this knowledge, it seems necessary that dental caries should no longer be treated solely by reparative means but that true prevention, by systemic treatment, should be instituted.

The teeth are often so seriously affected by caries during childhood that a number must be removed; thus such persons go through life with an impaired dentition, or, if pulp removal is resorted to, one or more possible sources of dental foci of infection are present. The dangers of focal infection may have been exaggerated by some, nevertheless there is still a real danger and this danger should be faced squarely.

The only certain way that dental foci of infection can be eliminated in the future and at the same time insure all persons a full complement of teeth, is to *prevent* the inception of dental caries.

In the future, the principal duty of the dentist will be, as it has been in the past, the repair of the ravages of dental caries and pyorrhea alveolaris. On the other hand, the responsibility for the *prevention* of dental disorders will rest on the shoulders of the medical profession. In this connection the dentist will be able to perform another valuable service, namely that of noting oral disturbances which may be reflected from incipient systemic disorders. Thus, the dentist who sees his patients in a state of comparative good health, can warn them of impending trouble and suggest a consultation with the physician. Observant dentists have frequently noted that their reparative dental work does not keep pace with the rate of dental destruction, and in despair they sometimes suggest to the patient a consultation with the family physician. This action is definitely the duty of the dentist. However, an attempt to prescribe should not be made by the dentist. This should be done only by the physician after a thorough physical examination in order to define the deficiency existing in the case of each patient.

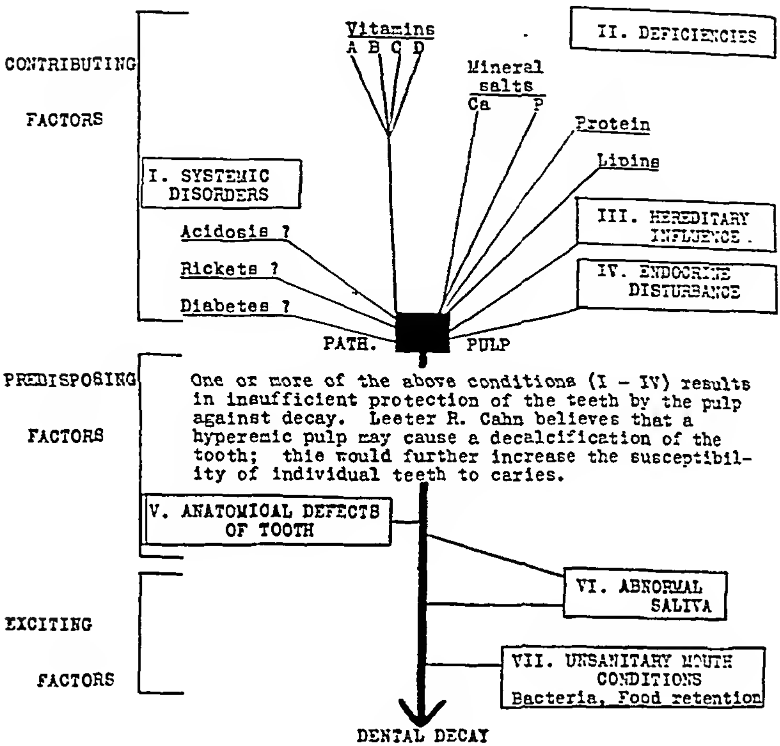
For a better understanding of dental disorders having a systemic origin, it may be advisable in future to create a new specialty covering particularly the borderline of dentistry and medicine. Even though it is uneconomic to train all dentists as medical graduates, it is advisable, nevertheless, to instruct a selected group of men in both fields of medicine and dentistry. Such men will be able to act as consultants and to suggest systemic treatment of general disturbances which are suspected of causing oral diseases.

There is evidence that rampant dental caries is a symptom of some systemic disturbance and it is suspected that pyorrhea alveolaris can be regarded in the same light. I have frequently referred a person to a physician for a

Fig. 6.

SOME POSSIBLE FACTORS INVOLVED IN THE CAUSE OF DENTAL DECAY

MOST ACTIVE DURING YOUTH



physical examination, and in many cases the condition of the patient was pronounced normal. However, in some instances, systemic disturbances were diagnosed some time after the first consultation. This leads me to believe that our laboratory tests, particularly in relation to the blood and the endocrines, are not sufficiently delicate to define some as yet unknown variation from the normal, which may exist in incipient systemic disturbances. The teeth, being farthest removed from the source of general nutrition, probably suffer first as a result of certain metabolic disturbances. Hence it is my belief that the teeth may at some time in the future be regarded as a delicate indicator of some phases of bodily health, even before a physical examination discloses any systemic derangement. This

view is by no means new, it was generally maintained during the last decades of the nineteenth century, but has been since disregarded as a result of the belief that the welfare of the teeth was not dependent upon bodily conditions.

Consequently, if we wish to prevent dental caries in children and young adults, and pyorrhea alveolaris in the middle aged and the old, systemic treatment must be instituted. For the purpose of defining such a mode of treatment, a more intimate association of physicians and dentists is necessary.

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DEATHS OF FELLOWS OF THE ACADEMY

Brown, James Spencer, M.D., Pinehurst, North Carolina; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1885; elected a Fellow of the Academy June 6, 1895; died, August 18, 1934.

Fishberg, Maurice, M.D., 1136 Fifth Avenue, New York City; graduated in medicine from New York University in 1897; elected a Fellow of the Academy January 2, 1913; died August 30, 1934. Dr. Fishberg was a Fellow of the American Medical Association and a member of the County and State Medical Societies, the New York Academy of Sciences, the American Ethnological Society, the American Anthropological Association and the American Folklore Society. Dr. Fishberg was Chief of the tuberculosis service at Montefiore Hospital. Besides treatises and articles on pulmonary tuberculosis, Dr. Fishberg wrote extensively on anthropological subjects and had made a special study of the Jewish populations of various countries.

Kilbane, Edward Francis, M.D., 40 East 61 Street, New York City; graduated in medicine from Cornell University Medical College in 1901; elected a Fellow of the Academy March 7, 1912; died, August 18, 1934. Dr. Kilbane was a Fellow of the American Medical Association and the American College of Surgeons, a member of the County and State Medical Societies, the American Urological Association and the Alumni Association of Lying-in Hospital. He was Associate Surgeon at Roosevelt, Genito-Urinary Surgeon at Misericordia, Consulting Urologist to Tuxedo and Flushing, and Urologist to Lincoln and St. Mary's Child Hospitals.

Tieck, Gustav John Eric, M.D., 2 East 54 Street, New York City; graduated in medicine from the Long Island College Hospital in 1899; elected a Fellow of the Academy October 6, 1910; died, August 18, 1934. Dr. Tieck was a Fellow of the American Medical Association, the American College of Surgeons and a member of the County and State Medical Societies. He was Director of otolaryngology at Broad Street Hospital.

Wainwright, Jonathan Mayhew, B.A., M.D., M.A., 327 North Washington Avenue, Scranton, Pennsylvania; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1899; elected a Fellow of the Academy April 7, 1904; died, August 3, 1934. Dr. Wainwright was a Fellow of the American Medical Association, the American Surgical Association, the American College of Surgeons, and a member of his County and State Medical Societies. For many years Dr. Wainwright had been Surgeon in Chief of the Moses Taylor Hospital in Scranton. During the World War he commanded a base hospital in France. In his later years he was especially interested in cancer research and since 1930 had been President of the American Society for the Control of Cancer.

OFFICERS OF SECTIONS AND AFFILIATED SOCIETIES, 1934-35

Dermatology and Syphilology, 1st Tuesday

Chairman	*Secretary*
RAY H. RULISON 145 East 54 Street	E. WILLIAM ABRAMOWITZ 853 Seventh Avenue

Surgery, 1st Friday

GUILFORD S. DUDLEY 27 East 63 Street	CONDICT W. CUTLER, JR. 667 Madison Avenue

Neurology and Psychiatry, 2nd Tuesday

C. BURNS CRAIG Neurological Institute	LEON H. CORNWALL 30 East 76 Street

Historical and Cultural Medicine

2nd Wednesday of November, January, March and May

RUSSELL L. CECIL 33 East 61 Street	JEROME P. WEBSTER 180 Ft. Wash. Ave.

Pediatrics, 2nd Thursday

HARRY BAKWIN 132 East 71 Street	ALEXANDER T. MARTIN 107 East 85 Street

Ophthalmology, 3rd Monday

WEBB W. WEEKS 20 East 53 Street	W. GUERNSEY FREY, JR. 121 East 60 Street

Medicine, 3rd Tuesday

RANDOLPH WEST 622 West 168 Street	PAUL REZNIKOFF N. Y. Hospital, 525 East 68 Street

Genito-Urinary Surgery, 3rd Wednesday

AUGUSTUS HARRIS 306 Park Place, Brooklyn	JOSEPH A. HYAMS 78 East 79 Street

Otolaryngology, 3rd Wednesday

MARVIN F. JONES 121 East 60 Street	WM. WALLACE MORRISON 39 East 50 Street

Orthopedic Surgery, 3rd Friday

LEO MAYER 140 West 79 Street	WALKER E. SWIFT 115 East 61 Street

Obstetrics and Gynecology, 4th Tuesday

HARVEY B. MATTHEWS 643 St. Marks Ave., Brooklyn	WALTER B. MOUNT 11 Seymour Street, Montclair, N. J.

AFFILIATED SOCIETIES

Society for Experimental Biology and Medicine, 3rd Wednesday

President	*Secretary*
A. R. DOCHEZ 136 East 67 Street	A. J. GOLDFORB City College, Convent Ave. & 139 St.

Harvey Society, 3rd Thursday

R. KEITH CANNAN Bellevue Hospital	EDGAR STILLMAN 22 East 69 Street

New York Pathological Society, 4th Thursday

PAUL KLEMPERER 385 Central Park West	IRVING GRAEF Bellevue Hospital

New York Roentgen Society, 3rd Monday

A. L. LOOMIS BELL L. I. Hospital, Brooklyn	C. WADSWORTH SCHWARTZ 33 East 68 Street

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EDITORIAL

TRANSVALUATIONS AND DEFLATIONS IN THE HISTORY OF MEDICINE AND ITS TEACHING

James Huneker once said that he loved music so well that he hesitated to disclose the seamy side of its practice, in other words, the caprices, professional jealousies and other humbuggeries of the virtuoso or prima donna temperament; which he recounted in "Melomaniacs" and subsequent fictions. Music is, in effect, the noblest and most *spirituel* of all the fine arts, compassing, as Goethe affirmed, the whole rhythmus of the inner life of man (*Andacht oder Tanz*). Heine even predicted that it will be "the last word of art." Stuart Mill, in his Autobiography, laments the approach of the time when all the possible permutations and combinations of musical sounds shall have been exhausted. In the chaos consequent upon the World War, music has clearly outpaced poetry, painting and sculpture in public interest and estimation. Where Walt Whitman or Vachel Lindsay had a moderate show of success in reading or reciting their own poems, people flock to endless concerts in vast numbers, and with an interest seldom apparent at an exhibit at an art gallery. Even the cacophonies of cubistic music are endured with the exemplary patience of dumb, driven cattle or the "sad civility" of lambs led to the slaughter pen. In New York City alone, the weekly output of public concerts occupies several columns in the Sunday newspapers. Radio has made the better sort of music a household word. The "canned music" obtainable by gramophone records is now approaching a high degree of permanent excellence and value. And in all

this, the composer has the distinct advantage. Beethoven projects himself into futurity by means of a crabbed, well-nigh illegible MS. score, say of a string quartet. Innumerable interpretations are possible. Nothing is of consequence unless the performance throws into relief the uncanny genius and *grandeur d'âme* of Beethoven, conveyed primarily on impersonal printed scores, now over a hundred years old.

The reading or delivery of medical lectures and papers might be defined as the virtuoso phase of the science and art of medicine. The impersonal, strictly scientific paper may be as dull or as dry as an official report or laboratory protocol; intelligible to a few experts only. No one cares, provided the findings and conclusions be accurate, well-considered and not too tedious in the reading or audition. When such a paper records a distinct advance, a worth-while discovery or invention, it becomes a small event in the history of medicine. That the portentous length of sundry medical papers bears a distinct relation to the high cost of medical periodicals is now a commonplace. That no specialist can keep up with the present proliferation of current literature on his subject is equally self-evident. The vast majority of current papers are in the nature of fertilizing media, "ploughed into the soil for compost," as Thoreau put it, and with "a good deal of guano in their destiny." Such slogans as "fewer and better periodicals" or "say it yesterday" are set off by the expansion of medicine in newer national groups or far distant countries. In consequence of the financial depression, there is no medical library in the world which can now afford to subscribe to more than a respectable fraction of current medical periodicals. The bane of recent medical literature is prolixity.

In the case of the innumerable papers read at medical gatherings, we have another matter. A recent observer classifies people, according to their perceptive powers, as visual beings (*Augenmenschen*), who apprehend by the eye; auditory beings (*Ohrenmenschen*), who learn by listening; and the general run of normal, well-set-up people

(*Muskelmenschen*), who acquire knowledge with effort, by grappling with it. There are experts who can estimate the positive value of a lengthy, complex scientific paper, as experienced readers take in the content of a prolix novel, by turning over the pages. In the case of lengthy abstruse communications of unfamiliar material, most of us have to "muscle-in." A test of visual capacity, favored by some European teachers of Latin, is to read a page or paragraph, close the book and state the content off-hand, in one's own language. A test of auditory capacity is what we actually grasp or retain of a lecture or a series of papers read at a medical meeting. As in Diderot's "Paradox on Acting," this turns as much upon the literary capacity, personal magnetism, elocution and expressive power of the lecturer as upon his auditors. As the mind wanders instinctively from a dry, dull page, so "cheerfulness, creeping in" is apt to distract attention from a boresome lecture, just as congregations gave themselves up to their own reflections during the stupefying sermons of the 18th century.

All this has important bearings upon the methods of teaching medical history introduced by Professor Sigerist in the Johns Hopkins Medical School, which constitute a new departure in this country. Heretofore, the subject had been taught by lectures alone. Chairs existed, with men of parts as incumbents, whose lectures were carefully prepared, usually from second or third-hand sources. The results were nearly always lamentable. The students, already overburdened with other courses, were bored and repelled by the dull quality of sentences intended for the eye alone, and by the unfamiliar names which Coleridge declared to be "non-conductors, stopping all interest."

There was apt to be an ominous shuffling of feet; students drifted away in groups as the lectures proceed apace; and, in some cases, the lecturer found himself, like the proponent of matrimony, addressing an audience of one. Even Billings' Johns Hopkins lectures of 1877-8, fashioned upon the old Daremberg plan (medicine as a succession of outworn theories) were in the nature of a "success of esteem" and were never published. In the case of some

visiting lecturers, President Gilman shrewdly resorted to the Chinese box plan of a succession of rooms adapted to audiences of decreasing size. Sigerist gets around this difficulty by carefully adjusting his material to the capacity and interest of freshmen, who are now much better educated than formerly; and by deploying the short, colloquial "chipped flint" sentence of Victor Hugo, Charles Reade and Emerson, which penetrates the ear. The subject is handled extempore, along broad lines, limited to essential phases only and illustrated by a minimum of lantern slides. Lectures to pre-medical students at Homewood (Dr. Oliver) utilize the historic approach to orient the prospective physician as to the responsibilities and pitfalls of his future career. But lectures will never carry the premedical or the freshman student very far in this subject. He is therefore brought into the seminary, where he participates in a general *viva voce* discussion of some theme, briefly exploited by the professor. In the seminary for advanced students, the professor activates, the students do the lecturing, as at the Harvard Law School; or prepare a collective wallside and glass case exhibit, illustrating the history of some such basic discipline as anatomy, pathology or pharmacology. There is nothing particularly new about the seminary method, which is employed in advanced courses of all going universities and was started long ago, in the workshops and training ships of the Naval Academy ("In the Navy, you don't learn how to do things; you go out and do them"). It was implicit in the programs of the medical history clubs and in Osler's plan of buttonholing the students in clinic to report on special topics at his home. Even urchins in the public schools of Washington were encouraged to gain confidence in themselves by describing their vacation experiences in their own language. But it is to Sigerist's lasting credit that, in two years' time, he has made the medico-historical seminary a going concern in this country. Ten years of experience at the Leipzig Institute have convinced him of the futility of burdening students or public audiences with more than essential data. A long succession of lantern slides, for instance, is apt to

confuse visual and auditory perception, particularly when the lecturer turns about to demonstrate his slides and cannot be heard. The aim is nowise "every man his own medical historian"; but to give the embryo physician a contact with the *humaniora,* which may be a permanent cultural asset or a sheet-anchor against boredom during the rest of his professional life. The germ implanted may enable the recipient to carry on in the same way with prospective pupils in the discipline or specialty he may be destined to teach. In keeping with the tenets of Diderot's famous paradox, a successful lecturer on a serious, scientific subject must never be mastered by his material, just as the real actor or virtuoso of music is never affected by the emotions he conveys. Disdaining meretricious, melodramatic devices or other vulgar gallery play, he must nevertheless have such unquestioned control of his material that he can deliver it from rough notes extempore, on short notice, even to the extent of adapting it, expanding it, compressing it or even curtailing it, to suit the needs of his particular audience. With the *coup d'œil* of an experienced general on an unknown battle-front, he must "respect his adversary" with a single eye to winning victories; in other words, so dramatize himself and his subject with reference to his auditors that he reaches them effectively and without effort. If he lectures above or below the capacity of his audience, he is lost. If he bores them, he is voted a "bromide," a "false alarm" or a "flat tire." Virtuosity of this kind is as rare among scientific men as it is among generals. There is still pith and pungency in Sir James Barrie's witticism, that the scientific man is the only being in the modern world who has something new to say and who does not know how to say it. Apart from specific talent or magnetism in the lecturer, the days of the didactic lecture seem numbered.

Advanced research work, fitting the student to be an independent investigator or potential teacher of medical history, usually takes the form of some special monograph, developing new knowledge, new viewpoints, new alignments, at the expense of the older stereotyped interpreta-

Handerson's translation of Baas (1876) and the organization of the Medical History Club of the Johns Hopkins Hospital, which turned out a long row of worthwhile contributions. Among the "high spots" of this period are the contributions of Osler, Jacobi and Robert Fletcher, Weir Mitchell's study on instrumental precision in medicine (1892), Alice Walton on the Cult of Asklepios (1894) and Billings' history of surgery (1895). The first series of the Index Catalogue (completed 1895) affords an almost complete lay-out of the older medical literature and became a permanent source for reference work. The period between the Spanish American War and the World War was one of new departures. The work of Sudhoff began to loom large and introduced novel criteria, viz., to challenge every accepted statement of fact, to verify at the source, to regard the history of a science as equivalent to the total fabric of the science itself (Goethe) and to mobilize thereto the data of anthropology, prehistory, numismatics, epigraphy and the rest of cultural history. The older text books of Daremberg, Haeser and Baas gave place to those of Withington, Neuburger, Pagel-Sudhoff and others who followed the newer trends. With the foundation of Sudhoff's chair and Institute at Leipzig (1909), medical history became a funded item in the university curriculum, where Haeser and Pagel had worked and taught without a budget. Sudhoff's *Archiv* (1910) sounded a clarion call, "To work, with pick and spade" and became a repository for serious, solid performance, as against amateurish bids for coin and *kudos*. In the United States, this was the period of the local medical history clubs. Doctors who had barely a bowing acquaintance with Hippocrates, Galen, Celsus or Paracelsus, began to turn out facile improvisations, cribbed as a rule from second-hand or second rate sources, and with a bogus assumption of omniscience as to the total range of medical history. Even in European centres, Sudhoff noted an occasional tendency to "throw out the chest" as an index of shallow qualifications. An ephemeral contribution to medical history came to be regarded as a convenient short cut to a permanent reputation not otherwise obtainable, as

if the subject itself were of immortal essence. But no great harm was done, since the general law of the medical history club was to shed assumption and maintain the attitude of the modest, willing learner. Osler once said to the present writer that as ambition is proportional to capacity, so serious accomplishment in this field would be conditioned by the selfless humility of the *bona fide* worker in science in facing a difficult problem. At the beginning of the 20th century, Packard turned out a history of colonial American medicine, based upon authentic research work. The subsequent period was one of general stimulation of interest and here the medical history clubs of Baltimore, Chicago, New York, Philadelphia and Boston distinguished themselves as activators of medical culture. Developments in the lake-shore and Pacific states were spontaneous, substantial and independent of Eastern or European contacts. The period preceding our entry into the World War was chaotic. In the twinkling of an eye, Europe became a congeries of armed camps and even poets, scientists and philosophers blossomed out *ex abrupto* as activators of hysteriform hate. The "Hymn of Hate for England" was set off by "A Song of Love for England," from an American lady. Germany was slapped upon the wrists by serious men of science, who affirmed that her scientific abilities and achievement were *nil.* We need not the satiric observations of M. André Siegfried to remind us that our own country, welded into organic unity by the Civil War and committed to the Washington-Monroe policy of independence of and detachment from other nations, was suddenly transformed into a noisy museum of ethnology, with the catch-word, "Find the American." Impersonal officials of the government were pestered to extinction by the obstreperous behavior of self-appointed antagonists and protagonists of warring races and nations. Espionage and hounding of commonplace, inoffensive people became, and still is, a monomania. Under such conditions, pursuit of medical history became of dwindling consequence, albeit sometimes made occasion for senseless racketeering. Throughout the whole insane welter, the Annals of Medical History (New York) served

as a neutral repository for contributions, irrespective of racial or national prejudice and the tendency of the historical to become hysterical.

The period following the great tragedy was one of war-weariness. Compelled to expend their total energies upon peripheral conflict at the expense of internal economy, the warring nations found themselves bankrupt. Prolonged wars of such dimensions bring in their train "red ruin and the breaking up of laws," an upheaval of existing social order and a total degradation of human dignity; as revolutions, even of honest intention, are apt to bring "the rats out of the cellar." The magnificent civilization of the 19th century Europe was smashed utterly. The greater classics of literature and music, which had inspired our youth, seemed insipid and, for a long time, came "uncouthly to the palate." American civilization was developed by "strong men with empires in their brains," set off by a few little seed-plots of cultivated people here and there, but the religious, ethical, social and æsthetic outlook of the great mass of the people was often limited, childish, small-town and provincial. The draft had revealed an unsuspected substratum of adults with undeveloped minds. To sustain sanity and morale in the trenches, it was necessary to keep cheery by the device of the prison-camps: *Il faut s'amuser.* A post-bellum generation arose, characterized by puerile mentality and childish personal traits. The play-boy, trivial, irresponsible, volatile and unreliable as a butterfly, was a wartime product, by no means confined to the United States. Reversion to the primitive and primordial in the fine arts (cubism, atonal music) was an expression of the fact that life itself had become aimless and meaningless. Composers became decomposers. The interest of Joyce's Ulysses is that it decomposes literary expression into its basic, primordial elements. The biographer became a valet to his hero, concerned with backstairs gossip and the seamy side of genius. The older school, who saw great men as moulded of their faults, were denounced as venerators of stuffed shirts, plaster saints and idols with feet of clay. The deterioration in quantity and quality of medical litera-

ture alone may be sensed by handling the volumes of the Index Medicus for 1913 and 1917-18. Its subsequent senseless proliferation is apparent in the volume for 1926. Nevertheless, the serious-minded remnant of cultivated Europeans maintained their culture in the face of extreme privation; and medico-historical research of high quality continued apace; to be reflected *longo intervallo* in such American productions as Cushing's Osler, Moodie's Palaeopathology, or Fulton's history of muscular contraction. A swarm of books on the general history of medicine appeared on both sides of the water, some in coarse vernacular or even doggerel. A feature of the playboyishness of the post-bellum period was the "smart Aleck" school of writers and the appearance of the medico-historical jokesmith, whose labored burlesques were concocted after the patronizing device: *Du sollst und wirst lachen.* The "humor" of these effusions was trite, forced, *gesucht komisch,* lacking in the essential element of surprise, in brief, as dismal and repelling as Blumauer's burlesque Æneid or a comic life of Christ. Here and there, medical history came to be exploited as a racket, to promote business enterprises or to advertise commercial products. Prime movers of medical education in the country were fain to regard the subject as a dilettante recreation of piffling importance, unworthy of an university chair. Sudhoff fulminated vainly about degrading the august Clio "to the level of the street-walker." "Medicine," he wrote, "is a sacred calling, and he who makes it ridiculous is guilty of sacrilege." Well-meaning enthusiasts, now and then, got up innocuous pageants, in the shape of a processional of medical heroes, beginning with the shadowy figure of Hippocrates. About this figure, we may linger for a moment to stress a point. Readers of the Jones-Withington bilingual, will recall the view of Wilamovitz that Hippocrates is essentially "a name without writings." All we know is that a leading physician and medical teacher of the name existed in the 5th century B. C. and was probably born on the island of Cos. Even the latter ascription is challengeable in the light of excavations, which go to show that the Æscula-

pian cult became associated with Cos *after* the presumable death of Hippocrates. Nevertheless, the cult may have been established there in his honor *post mortem* and along with it the library or collection of scriptures known as the Hippocratic Canon. Each of these writings now "dates," in the sense of being roughly assignable to some period before, during or after the estimated life-span of Hippocrates. In the second and third groups are certain incomparable texts, which are either the product of some great mind or of a school of thought inspired and activated by such a mind. If we agree to designate the vague authorship of these Coan texts as *X*, then it is convenient to equate X with Hippocrates, whom Alexandrian tradition placed *primus inter pares* with Praxagoras and Chrysippus as an authority on Dietetics. The gradual deification of Hippocrates, as *Heros Iatros*, by the Alexandrians, by Celsus and by Galen, up to the time when Hippocrates supplanted Galen himself, has been elucidated by Edelstein. This heroizing or canonizing process has been continuous, from the legendary transfiguration of Asklepias by Zeus, to date[1]. Could we now recede backwards in time, upon a ray of light, and grasp the true inwardness of the Hippocratic mystery at the source, we should probably find something utterly different from the conjectures of the romantic school or the realistic school. A large segment of Greek medical literature is as irrecoverable as the lost tragedies of Æschylus. The earliest known Hippocratic MSS. were copies made some fifteen centuries after the Hippocratic period. Classical philologists, nevertheless, have drawn illuminating conclusions from detective work on these fragmentary remains, and not entirely as *le pain des professeurs*. In such work, the location of the ugly little fact destined to slaughter a beautiful hypothesis may be likened to the study of a spirochætal organism under the microscope.

Around the periphery of the eyepiece, an infinite number of futile viewpoints may be possible; but visibility is largely a matter of focussing. Even so the creature may be so

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1 For exposition, see: H. E. Sigerist: On Hippocrates. *Bull. Inst. Hist. Med.*, Baltimore, 1934, II, 190-214.

elusive in its shiftings and windings that only an approximate notion of its actual shape and size is possible. At the farewell banquet tendered President Woodward, on his retirement from the Carnegie Institution of Washington, there was a clever burlesque of the all-too-human tendency to distort the significance of historic occurrences to suit the whims and personal equation of the historian. No two witnesses can describe an exciting occurrence, let alone a tedious, lengthy episode, alike. After the World War, the General Staff of the Army required that every declarative statement of fact in a historic narrative be verified by documentation. The medical historian is on delicate ground directly he deserts the simple military rule: Facts, not opinions, are wanted. In the matter of opinion, one might alter the witticism of Philip Guedalla: As history repeats itself, medical historians are apt to repeat one another. One of the leading medical thinkers of England, upon hearing the net result of original investigation in medical history during the last 35 years, turned sadly away with the remark: "In view of the abyss into which present-day Europe seems sliding and the duty of getting sick people well, it surely does not amount to much." The medicine of the future is by way of being profoundly affected by social and economic change and it is probably more rewarding to visualize the significance and mass-action of such movements than to fumble over insignificant details in the lives of men. Our knowledge of the life-histories of ancient Greek physicians is in what the mathematician Boltzmann called "a highly improbable state." What will be known of the most prominent figures of our own time, a few hundred years from now, is even more dubious. Nevertheless, accurate verification of existing facts and dates at the source is one of the most important functions of medico-historical investigation. Rowntree made a complete revision and expansion of the meagre details in the life of Parkinson by going over the records in London. Whether the history of medicine should be pursued as a branch of dry science or as an all-embracing phase of the general history of culture is a large open question. The known criteria of a scientific

proof should undoubtedly be applied to the specific problem and in a spirit as austere, impartial and impersonal as that obtaining in a physical or chemical investigation. But the general subject touches human life on every side and every case the doctor handles is, first of all, a human and humanistic problem. The art or bedside practice of medicine, which in Edelstein's reading, was naught but a mechanical, rule-of-thumb craft (*techne*) among the peripatetic physicians of ancient Greece, is, in every respect, a fine art, bound up with ever-increasing experience of human nature. This is the permanent ideal of the medical profession, that the natural born bedside doctor makes his knowledge out of his own experience, with some reliance on books. Not so long ago, the view obtained that medicine may be merged into chemistry or physics or, as Virchow opined, be absorbed in the general body of common knowledge and vanish as such, like Huneker's orchestra disappearing into the fourth dimension of space. But there are no immediate signs of either phenomenon. The view of Sarton that the history of medicine is to be envisaged and treated as a subsidiary phase of the history of science is the view of an essential mathematician. The doctor's rôle in the matter will never be understood in this way. That the observational methods of clinical and biological investigation are implicit in the Hippocratic scriptures was recognized by observers so different as Aristotle and Helmholtz. Apart from the mathematics, Greek medicine, in the older view, was the foster-mother of European science. The glory of Greek medicine is irradiated in the sentence of Plato: "He shall be as a god to me who can rightly discriminate and define." Come what may, the formative period of activation, stimulation and proclamation is by, the movement for substantial research is forward, and, with this objective, the little barque of medical history must take its chances upon a stormy sea of sinister currents and cross-currents, concerned with no less than the hatching of wars and revolutions, the undermining and overthrow of governments, the enslavement of peoples and the disruption of any honest social order whatever.

F. H. GARRISON.

THE CAUSES AND PREVENTION OF BLINDNESS*

ARTHUR J. BEDELL
Albany, N. Y.

We are gathered together this evening to do honor to the memory of Hermann M. Biggs, a leader of men, a dreamer of dreams, a skillful administrator and a competent authority to whom his associates looked for inspiration and guidance. Biggs was endowed with unusual executive ability. He expended his energies in acquiring special knowledge, which he immediately applied to the advancement of public health. It is a privilege and an honor to take part in perpetuating the name of one who did so much for the commonwealth.

The causes of blindness, partial or complete, are numerous and vary so much as to the time of life when they become manifest, the severity of effect and amenability to treatment, that a comprehensive survey should be made before their prevention can be adequately discussed.

Inherent in the genes of male and female are certain unmeasured potentialities, which may be expressed in abnormalities during intra-uterine growth or at any other time during the life of the individual, and although some of these may be altered by environment, conditioned reflexes, a great many are fixed and constant.

The prenatal stigmata include those which result from the lack of normal development, such as an arrest in the fusion of the ocular cleft or the imperfect growth from the anlage resulting in monsters. The investigation of these anomalies offers an excellent field for medical research. The eugenic societies, as soon as their field expands and their recorded observations become more numerous, will, I am sure, give added attention to these defects.

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* *Hermann Michael Biggs Memorial Lecture, delivered at The New York Academy of Medicine,* May 3, 1934.

Among the manifold problems in the prevention of blindness, those arising in the practice of obstetrics play a striking part. Just at this time the natal conditions are the subject of much acrimonious discussion. Some commissions, I fear, expect the most perfect surroundings for all births and the most expert special treatment. This is Utopian. We approve of any attempt to better the obstetrical care of the women of the United States for our maternal mortality rate is high.

Pregnancy, although biologically a desirable and necessary condition, is nevertheless one which produces a marked change in the maternal organism. Most women carry the child and are delivered normally without any detrimental systemic changes. There are, however, an increasing number of pregnant women who show evidence of toxemia, the earliest signs of which are found in the fundus of the eyes as spasms of the retinal arteries. The irregular narrowing of the lumen of the minute retinal vessels is proof of impending disaster. Comparatively few physicians realize the importance of this premonitory sign. All obstetricians agree that undiscovered or untreated toxemia of pregnancy is a serious condition. Ophthalmologists know the value of frequent ophthalmoscopic examinations whenever visual disturbances are reported. If the early signs of vessel spasm are not recognized and if the appropriate treatment is not promptly instituted, the contraction becomes fixed and the patient never recovers from the damage to her retina and general circulatory system, for when the high blood pressure of toxemia becomes established it resists all medication. The recognition of the eye changes is imperative if the vision is to be preserved and life prolonged. Because patients often fail to observe or to report symptoms of ocular discomfort, the physician should always inquire regarding these possible complications.

It is well to realize that the sight may be permanently lost or seriously impaired as a result of an abortion, when a minute clot is dislodged from its primary location in the uterus and lodges in the central artery of the retina.

Many babies become blind through an infection of the lining membrane of the eyelids acquired during passage through the birth canal. This is the direct consequence of organisms growing on the conjunctiva, producing a fulminating inflammation with extreme swelling and redness of the eyelids. At the onset there is a watery discharge from the eyes which is soon followed by a profuse purulent flow. It should be clearly understood that the inflammation of the eyes of the newborn is by no means always of venereal origin but may be and often is the result of other pus producing cocci and bacilli.

The birth of the baby may be retarded by mechanical or other forces so that operations become necessary. The delivery by forceps may cause serious damage to the eye when the blades compress the eyeball and stretch or rupture the cornea. The instrument may also dislocate the eye or even produce sufficient traction to interfere with the function of the optic nerve.

Intraocular hemorrhage in the newborn is found after normal delivery, after the use of forceps or after a Cesarean section; so that it should not be ascribed to the trauma of birth. The after effects of such hemorrhages are the subject of many investigations. An opinion was recently expressed that they may be the cause of some scars in the retina and choroid which have never been clearly understood.

An infrequent but terrible cause of blindness is xerophthalmia induced by the lack of essential food elements. This becomes evident shortly after the birth of a seemingly normal infant. The cornea literally melts away and in a few days the patient is hopelessly and incurably blind.

If the baby has passed through the dangers attendant upon his birth, it may be found that his eyes are not perfectly developed and that some congenital defect will handicap him for life. He may be without eyes, or the eyeball may be too small, or too large. The globe may be elongated producing extreme short-sightedness with stretching of the retina and choroid and traction on the optic nerve; or it

may be too short with an extreme degree of far-sightedness; or the eyes may turn far in, out, up or down.

Some parts of the eye which normally disappear before birth may remain as a pupillary membrane or a patent Cloquet's canal. Occasionally, extremely large blood vessels, angiomas, destroy sight.

If the infant is fortunate enough to have no congenital malformation, he may have an inherited constitutional disease which proves to be most destructive in its effect upon his eyes. Syphilis is the activator in most of these tragedies. In specific interstitial keratitis, the child complains of photophobia and soon enters the stage of unilateral or bilateral vascularization and infiltration of the cornea. After several months of treatment, the cornea may become clear and vision be restored. Many patients are not so fortunate, the cornea remains hazy and the sight so poor that they are unable to care for themselves and become public charges or burdens to their families.

Some cases of congenital syphilis are diagnosed when a bilateral swelling of the knees precedes a red eye, at or shortly after puberty.

Congenital optic atrophy may be produced by syphilis. An unique disruption of function is called hereditary optic atrophy. This clinical entity is seemingly an abiotrophy with familial traits. In a recent report, I presented a family tree of five generations in which several members lost most of their sight a few weeks after a sudden reduction in vision. The individual episode was unaccompanied by any pain or redness and was without any general or local signs of trouble.

The line between the congenital and the acquired eye diseases cannot be clearly drawn. A cataract is an opacity of the lens or its capsule. The congenital cataract is usually of the lamellar type showing as a grayness of the pupillary area. This may be sufficiently dense to attract attention at birth or it may not be noticed until the child is many

months old. Therefore, we have families in whom cataracts are congenital, others where they develop in early childhood and many in whom they are the trial of advanced years. There is no question but that the tendency to cataract is inherited. Laboratory experiments and clinical experience supply abundant proof of this assertion.

Whenever you think of a cataract always have an exact understanding of what is meant by the term and especially what part of the lens is involved. By use of the slitlamp, a combination microscope and narrow beam of intense light, we are able to tell how old the patient was when the cataract developed. It is also possible to determine whether the cataract is stationary or progressive and if the latter how rapidly it will advance. In addition to this information so vital to the ocular life of the patient, we can decide whether the cataract is the direct result of a known agent or secondary to an intraocular disease. Numerous clinical facts must be searched for and appraised in the study of a cataract.

The subject of cataract is, therefore, of engaging interest. It has lately been determined that opacities in the lens may form as a result of the hypersecretion of some of those mysterious bodies called glands of internal secretion and that the hyposecretion of others, such as the thyroid, parathyroid and pancreas may produce somewhat similar changes. It seems fair to state that with the exception of a rare type, which appears in children suffering from diabetes, that the most universal cause of acquired cataract is age, and by age I do not mean chronological but physiological senility. Everyone should know that if he lives long enough he will have some opacity in the lens, but it must be repeatedly stressed that the mere appearance of a lens cloud is not sufficient reason to tell the patient that he has a cataract for it may never interfere with sight. If he has to be told, then time should be taken to explain his exact physical condition and the manner in which it will influence his future life. Bear this in mind when we discuss preventive measures.

There is evidence that hardening of the eyeball, glaucoma, can be definitely traced through families, and I believe it is conceded by the most competent internists that high blood pressure, kidney disease, arteriosclerosis and diabetes have their inherited types. Ophthalmologists believe that the tendency to cataract, glaucoma, extreme degree of myopia, strabismus and certain degenerations in the macular retina are inherited.

On the other hand, sufficient testimony has been offered to uphold the contention that glaucoma may be acquired for isolated cases are found in families in whom no previous one has appeared. The exigencies of modern life, worries, anxieties, lack of the necessary mental equilibrium to adjust oneself to the rush of the times, all seem to have an influence in initiating an attack of glaucoma. Much time could be devoted to this subject which is of vital interest to everyone for no race is exempt, no person immune and all are susceptible whether male or female, far-sighted or near-sighted, those with high or low blood pressure, with or without arteriosclerosis, a celibate or a roué.

Two definite types of glaucoma are recognizable, one is often ushered in by an attack of nausea and vomiting, an acute gastrointestinal upset. The eyeball is darkly congested and the pupil dilated with rapid, serious obscuration of vision. This may have been preceded by times of partial fogging or dimness of vision or even premonitory periods of transitory blindness.

The other type is one of the most serious of all eye diseases because of its insidious onset with lack of redness and absence of nature's signal of alarm, pain. It may destroy sight or greatly constrict the field of vision before its presence is suspected. Few eye conditions call for more discriminating, diagnostic acumen than the early recognition of this common destroyer of the sight of the mature and aged. I cannot refrain from expressing the admonition that glaucoma of this type can only be diagnosed by ophthalmoscopic, field and intraocular tension studies. The last portion of sight to be destroyed is central vision. Fre-

quently the patient is unconscious of the slow, continuous degeneration until something makes him cover one eye and then he discovers his poor sight. Thousands and thousands of people are suffering from this disease, which although most frequently manifest after forty, may be present at any age.

Our manner of living tends by the very nature of our existence to demand the expenditure of more and more physical and mental energy. If a person who is unable to adjust himself to conditions marries and has a family some of his descendants may give evidence of this lack of stamina by early degenerative changes.

A comprehensive study of those who die of hypertension seems to substantiate this belief as each succeeding generation dies earlier than the preceding one. There is an apparent increase in the cardio-vascular-renal diseases and many patients go blind from embolism, a sudden closure of a retinal artery, thrombosis, a rapid occlusion of a retinal vein or retinal hemorrhage. The number of patients suffering from hemorrhages inside of the eye is alarming.

Even when these red flags of blood are prominently displayed, many fail to, or cannot, heed the warning and as a consequence die from a cerebral hemorrhage, which might have been postponed for years.

A class of diseases which is on the border line between the congenital and the acquired includes a curious degeneration of the retina, retinitis pigmentosa, the easily recognized symptom of which is night blindness. This is not only inherited but it also develops in those undernourished as after periods of prolonged fasting. The rare angiomatosis retinae, a disorder of eye and body characterized by the formation of angiomas and cysts is probably also familial, as is corneal dystrophy and keratoconus where the sight is so reduced as to constitute veritable blindness.

The list of inherited possibilities is lengthy but when compared with those that are acquired it is really very short.

Focal infections, syphilis and tuberculosis hold the attention of all interested in the most prolific sources of blindness.

A focal infection is a localized area of disease which may produce remote systemic effects. In the eyes it may initiate an iritis, a choroiditis or a retinitis with secondary optic atrophy ending in blindness. The teeth, tonsils, nasal sinuses, intestinal tract and the genito-urinary organs may be the site of the original trouble from which the toxins are absorbed.

Syphilis may destroy sight by its action on the blood vessels as in choroiditis or by direct effect upon the nervous system as in locomotor ataxia or general paralysis.

Tuberculosis may involve any part of the eye and is a prevalent disease, frequently encountered in seemingly healthy young adults. Often it demands the most searching investigations to uncover its presence for the vast majority of ocular tuberculosis is unassociated with pulmonary invasion. The cornea may be involved in the form of interstitial keratitis, the iris in an intractable inflammation, the retina and choroid in a destructive process with single or multiple lesions or there may be recurring intraocular hemorrhages.

In the light of our present knowledge a phlyctenule is an allergic reaction of tuberculosis. When the cornea is the site of the lesion, the dread of light is extreme. Repeated attacks so cloud the cornea as to materially reduce vision, not only directly by the scar, but also indirectly by leading to the development of near-sightedness. The differential diagnosis between syphilis and tuberculosis of the eye is sometimes very difficult. The decrease in the number of people suffering from active or open tuberculous lesions is worthy of note. Perhaps the chronic forms are, therefore, more apparent.

In this country leprosy is too rare to need consideration in this address.

The infectious diseases of childhood have for the time lost much of their virulence. Diphtheria is readily controlled by antitoxin, small-pox prevented by vaccination and when scarlet fever is responsible for the eye trouble, it is because of kidney complications. There is a possibility that an attack of mumps may induce an optic atrophy. Because conjunctivitis is one of the early symptoms of measles, its importance as an agent capable of impairing vision has been over-emphasized. I have never known blindness to result from measles.

Trachoma is still an active agent in producing poor vision and in destroying sight. All physicians understand the clinical course of red eyes, discharge, photophobia, corneal ulcers, corneal scars and distorted lids. In some sections of this country trachoma constitutes a serious health menace.

The chemicals of industry are potent factors in reducing vision by damaging the optic nerve although they rarely produce total blindness. They include lead and some of the carbon compounds such as the tetrachlorid used in cleaners' and dyers' establishments and disulphid. The excessive indulgence in alcohol and tobacco by the susceptible may terminate in imperfect vision.

Quinine taken in large doses especially as an abortifacient has permanently destroyed the function of the optic nerves.

There are several blood states such as pernicious anemia and leukemia during the course of which retinal hemorrhages and infiltrations of the retina may injure or extinguish sight. Unusually rare incitants like certain skin diseases, lipoid deposits and lack of the essential mineral elements such as calcium and phosphorus may also damage vision.

Degeneration of the macula is a common condition produced by the closure of the blood vessels supplying nourishment to that sensitive part of the retina. The patient loses central vision but does not go blind from the disease. The

appreciation of this fact has proven of immense comfort to the aged sufferers, many of whom have looked forward to advanced life as a time for concentrated reading and who when deprived of this long anticipated pleasure are terribly worried and fear complete blindness.

Detachment of the retina, usually a sudden separation of the retina from its choroid base, may follow an accident or develop in a seemingly healthy eye although it occurs much more often in a near-sighted one. The patient sees only part of an object and the eye remains unchanged in outward appearance. Only a skillful physician can distinguish the different kinds of retinal detachment. One form is coincident with the expansion of an intraocular tumor, but, fortunately, most detachments are not caused by such a calamitous condition.

There are three forms of malignant disease which attack the inside of the eye. The one we have just mentioned is sarcoma of the choroid, found most frequently in adult life. The earliest stage can only be detected in the course of a routine ophthalmoscopic examination when a small elevated mass can be perceived. The second stage is manifested by a defect in the field of vision. The patient becomes conscious of a haze or cloud which partially obscures his sight. Obviously this loss is more quickly recognized if the growth is in or near the center of vision. The third stage is characterized by an intense redness of the eyeball, marked decrease in vision and excruciating pain. The fourth, or terminal stage, is that in which the tumor penetrates the eyeball and appears between the eyelids or if it has extended into the orbit, pushes the globe forward. At this time, there is usually a metastasis somewhere in the body and the prognosis for life is hopeless.

The second intraocular growth occurs only in children and is called glioma of the retina. Here again the first signs are ophthalmoscopic but as the tumor increases there is a curious almost pathognomonic yellowish glare from the pupil. If not correctly diagnosed and treated at this stage, the mass continues to enlarge both anteriorly and poster-

iorly. If the backward extension is the more rapid, there is involvement of the brain with secondary meningeal symptoms followed by death. If the progress is forward, a large bleeding mass fills the orbit, involves the cheek and the patient finally dies from inanition.

The third form is carcinoma. This is not only rare but its progress is capricious and its extensions more bizarre than either of the other two.

Although the eyes are protected by the overhanging bony orbital ridges, the eyelids and the eyelashes, many are injured. The largest number of accidents are caused by flying particles such as emery, iron specks, steel chips, pieces of copper, splinters of wood, cinders, glass or brass. These frequently lodge in the cornea and if they become infected or if they are unskillfully removed a corneal ulcer may develop with secondary loss of vision. If a foreign body inside of the eyeball is not removed, there is grave risk of sympathetic ophthalmia. This is a very strange condition in which the eye that was not injured becomes affected and the process terminates in partial or total blindness.

In our present complex life the eyes are exposed to chemical burns from battery fluids, lime, corrosive acids, ammonia fumes, sulphur dioxid, and tear gas. Many hunters, policemen, state troopers and innocent on-lookers are injured by explosive fire-arms and air-gun shots. Many eyes have been severely damaged and some destroyed when struck by tennis or golf balls.

The eyes of hundreds of children have been lost after an injury by toy arrows, spears and sharp sticks, by scissors used to untie a refractory knot in a shoelace, by whittling with a jack-knife drawn toward the face and in many other accidents. Automobile casualties are responsible for many blind eyes as a result of fracture of the skull, laceration of the eyeball or even evisceration.

Any penetrating wound of the eye may produce a cataract or start an infection which if unchecked ends in a deep abscess, panophthalmitis, necessitating the enuclea-

tion of the eyeball. A severe compression of the globe may also initiate a cataract or tear the choroid. Prolonged exposure to great heat is responsible for the peculiar kind of cataract found in glassblowers and puddlers. The destruction of the macular region may follow excessive exposure to brilliant sunshine especially when reflected from the snow or when a solar eclipse is viewed without sufficient protection. The macula may be damaged when a worker using an acetylene torch fails to wear his goggles.

The classification of industrial accidents and hazards has been summarized by many commissions. We register one caution in regard to accepting the accuracy of statistical information derived from Compensation Board reports, namely, the amount of ocular damage does not always correspond to the percentage loss of vision on which the award is made.

A facetious writer might start the next paragraph with the heading, "What Price Beauty?" The sale of cosmetics has reached enormous proportions. Some beautifiers are most destructive in their action. "Lash-lure," an eye-lash dye has been reported to have produced marked inflammation of the eyelids, the conjunctiva and the cornea and it is conceivable that if such an activating agent is not recognized and its use discontinued, blindness may ensue. Some hair-dyes have a similar deleterious effect.

Coincident with the changes in feminine apparel, there has been a widespread demand for depilatories and consequently some very harmful ones have been placed on the market. The thallium containing mixtures such as Koremlu have precipitated a general inflammation of the peripheral nerves and when the optic nerve is involved, the patient often becomes blind.

Fortunately, we live in a progressive age when medical men are fully aware of their tremendous responsibilities to conserve vision and prevent blindness by caring for the baby, the child, the mature adult and the senile. A comprehensive program for the prevention of blindness should have as its activating, inspiring leaders ophthalmologists,

obstetricians, physicians, broad-minded conscientious educational authorities, public health agencies, the nursing and sociological forces and the eugenists. The plan and purpose of this work will continue to broaden as it has since its inauguration by the Medical Society of the State of New York. To accomplish the most good and advance the program farthest, we must understand that there is no demand for a revolution in the practice of medicine, there is no need for a cataclysmic upheaval or for displacement of anyone in the medical group and no reason for the injection of artificial stimuli by new or old pseudo-medical lay organizations, but there are excellent reasons for enlisting all interested in the actual bonafide warfare in a mass attack for the eradication of blindness under the direction of organized medicine.

As we have noted that the eyes may be damaged before birth, we should initiate and carry through a campaign for the enactment of a law making it mandatory on everyone who wishes to marry that they be examined and found free from active transmissible infections like gonorrhea and syphilis. This is neither a theoretic nor impossible measure.

Much is being written but less said regarding the necessity of sterilizing the unfit. Those interested in the reduction of certain types of congenital blindness are urged to support proper legislation directed toward the biological improvement of the race.

In the enlightened portions of New York State, there is little need for an active campaign to arouse the interest of the mother in the health of her expected child. There is, however, and I fear there always will be, the necessity for constantly telling thousands of prospective mothers what prenatal care means to them and their babies. For example, it is conceded that if a mother is syphilitic, her child can be immunized if treatment is started early in the pregnancy.

The attending physician can by the dissemination of this information and the application of therapeutic measures greatly aid in the control of maternal syphilis. Interstitial keratitis would then be reduced and some day it might be

abolished. Furthermore, it has been demonstrated that syphilis is a cause of hereditary dystrophies and deformities. Therefore, many of our congenital ocular defects might be materially influenced, perhaps to a greater extent than some of us dare hope.

Syphilis is a menace to the eyes of persons of all ages and the problem of control is most complex, involving so many customs, convictions and emotions that it seems well nigh impossible to lessen or remove the scourge. Because of these various barriers, the forces of justice and health must continue to present a united and a stronger front to conquer the vile destroyer of sight, happiness and even life. Legislation will not remove the pestilence. Sometime ago in a discussion of blindness a proposition was presented that everyone should have a Wassermann test and further that they should be retested at the end of definite periods. It is fortunate that no one has tried to enforce such a scheme for it would tend to nullify some of the good that is being accomplished by the more extensive use of the diagnostic serological methods. The positive Wassermann reaction occasionally indicates something other than syphilis and the reaction may be negative even when syphilis is present. The registration of a syphilitic by name is most distasteful to me and surely the field of control could be enlarged if the report was submitted without name or address. This is not a new proposal for the method has been used successfully in some parts of the world.

No one can question the fact that the mother must be well nourished if she is to bear a healthy child, but we must remember that what is adequate for one group may not be sufficient for another and that approved hygienic surroundings during the puerperium are subject to wide variations. An attempt to standardize home, food and care will, I fear, delay or even defeat the purpose of those who are laboring to improve the status of American motherhood. The obstetricians can be relied upon to prescribe the necessary food elements for the proper development of the newborn and the maintenance of the mother's health.

In 1881 Credé, a practicing obstetrician of Leipzig, made the announcement that it was possible to materially reduce the incidence of the blindness of the newborn. His revolutionary procedure was accepted by the medical profession of the entire world and in 1887 the members of the Medical Society of the State of New York started an active campaign for the promulgation of his discovery. Since that time, many organizations interested in the prevention of blindness have contributed their part in spreading the gospel of prophylaxis.

As soon as the baby is born, the eyes are wiped with a soft cotton swab, bathed with boric acid and two drops of a 1 per cent nitrate of silver solution instilled into the conjunctival sac, not on the cornea. If there is more than a transitory silver reaction, special care must be taken to keep the eyes clean and the services of a competent eye specialist secured. Although in many states some method of prophylaxis is mandatory, the exact medication is left to the discretion of the attending obstetrician. This, I believe, is unfortunate, and although I am opposed to prohibitory regulations and rules, I have repeatedly urged the exclusive use of nitrate of silver, for probably every other drug has at one time or another proved inefficient. This method of preventing ophthalmia neonatorum is taught to every medical student and every midwife so that now there is less danger of the infection than formerly. The rigid enforcement of this important measure must be continued.

When the infant shows any signs of malnutrition, extra care must be taken to prevent xerophthalmia, which can in most cases be checked if promptly recognized as a destructive corneal lesion and not considered a mild conjunctivitis until it is too late to save the cornea.

The baby who is born without defects must be constantly guarded, for eternal vigilance is the price of normal sight.

If those associated with children knew how to instruct them in the correct methods of play, it would be possible to prevent many accidents. Some parents object to their child wearing glasses. They fear that his eyes will be injured.

Millions of children wear glasses and the number of eyes that are cut when the lenses are broken is extremely small; so that it does not constitute a serious risk. Heavy cumbersome, non-shatterable glasses are now obtainable but because of their weight they annoy the wearer and he discards them at the time when they are needed most. In some communities the air gun has received its proper legal condemnation. The prevention of accidents to the eyes of children should constitute an important continuous part of any crusade against blindness. The spasmodic Fourth of July scare is helpful but too limited in scope.

I know of few preventive measures which pay larger dividends of satisfaction than the early, efficient, skillful care of injured eyes. If everybody understood that such eyes do not require an instantaneous diagnosis and treatment, many which are now lost might be saved. At the time of the accident, the eye should be covered with a clean cloth and the specialist who is to attend the case carefully selected. Before an injured eye is removed, it is advisable to have a consultation. The danger of sympathetic ophthalmia is real, although modern, efficient treatment has greatly lessened its incidence.

Many agencies have combined to protect the worker in hazardous occupations. The machines are guarded, the illumination sufficient and goggles are used in all properly supervised factories.

The lighting of home and school room has been improved immensely as a result of the almost universal use of electricity, but there are many details such as nearness to the source of illumination, the strength of the electric bulbs, direct and indirect lighting, the reflecting background, the color of the light and the position of the reader or worker which call for more investigation.

How many of you know that you can telephone to your local electric light company and ask them to send an inspector to check over the lighting of your home? A competent investigator will accurately measure the amount of light needed in every room and for every purpose. This service

was instituted by the Niagara Hudson Company about seven months ago and has already received widespread endorsement. When you get home ask if your company is doing this, for I am sure that if it is not the management will be glad to do so as soon as it appreciates that you wish it. This is an example of true public spirit as applied to the conservation of vision.

Do you fully appreciate the necessity of a careful, complete physical examination of every child before he enters school and have you seriously considered that the family physician is the most important link in the chain which results in the development of a good citizen? And I wonder how many public health workers can explain their recommendations for free dispensary service when they know that the child should go to a private physician's office? To that crowd and others who are attempting to foist new methods of practice upon the medical profession, I wish to call attention to the fact that this is still the United States of America. Experiments and experience have proven the futility of trying to engraft foreign methods of group herding upon the liberty loving people of America. I sincerely hope and pray that individual effort will always remain as our guiding national inspiration and that those who are influenced by selfish motives to attempt the implantation of mass socialism may be exposed under the brilliant, searching light of a reawakened individualism.

The pre-school child must also be examined and the ideal place for this is the family physician's office. Concentration on this activity will prove to be of inestimable value not only as regards eyes but also general health.

The prevention of considerable blindness rests in the hands of the obstetrician and the pediatrician for the trouble may develop before, during or immediately after birth.

It is important that diseases of the eye be recognized as early as possible. To assist in this, the inspection of school children became one of the functions of the New York State Education Department in 1913. Every child in a public

school is supposed to have his vision tested once a year and if an imperfection is found by this superficial test, the parent or guardian is notified. These inspections have revealed a great many eye abnormalities and saved some children from blindness. Raising the morale of the child with defective vision by improving his sight has materially helped the teachers to get better results from their instruction. A school inspection is not an examination. Many children who need expert eye care are overlooked in the school test. This should be stressed and explained for too many parents believe their children's eyes are normal simply because they happen to read a given line of letters.

School inspection like all mass medical examinations is sometimes open to criticism but it is the best procedure which can be proposed at this time. The parochial and private school children are not always included in the scheme so that a large percentage of our growing youth do not receive the benefits of this cursory investigation.

It is often said that too many eyeglasses are prescribed. That is admitted but who is to tell when a patient should have glasses, a trained medical observer or a seller of lenses?

When a child is found to have uncorrectible, defective vision of such a degree that he cannot see the usual type of the text book, he should be admitted to a sight-saving class. If the defect is so great that he cannot even see special work, then he must be taught in a private or state school for the blind. Sight-saving classes are in many places a dumping ground to which the mentally defective, hard of hearing and incorrigibles are sent. Those interested in the prevention of blindness should assert themselves at this time and insist that no one is admitted to a sight-saving class for any other reason than poor vision. A critical inquiry will prove that this reasonable suggestion is most timely. A child who has one eye with normal or nearly normal vision should not be placed in such a class for he soon considers himself handicapped, and may by his inability or unwillingness to work become a state charge. In this connection, I

sometimes wonder if social workers are more interested in statistical tables than in the application of the laws inscribed on the ancient mosaic stone tablets.

Medical inspectors frequently encounter cases of cross-eye. Remember that a turned eye is either already poor-sighted or will become so unless corrected. The earlier the child is placed under treatment, which consists of accurate testing for glasses under "drops," occlusion of the better sighted eye, exercise and operation; the more satisfactory the result. Glasses can be worn as early as the first year of life. Don't procrastinate. Thousands of young men were rejected for full service at the time of the World War because of unrecognized or ineffectually treated cross-eye. The economic importance of the cosmetic blemish and crippled sight is appalling.

Rapidly progressive myopia must be considered as an individual problem. The most skilled care is required, no mass treatment will suffice. Every parent must be taught that long delay is dangerous, poor care costly and cooperation essential, for, if the child does not wear the glasses nothing can be done to control the progress of the disease.

Early adult life is a period of great danger because of the intermingling of the sexes. Vicious movies, degrading exposure and lack of moral control, especially when under the influence of alcohol, when removed from proper home restrictions or when tempted by those about whom the Proverbs of Solomon raise warnings and protestations, all play an important role in disseminating disease.

The greatest extension in the field for prevention of blindness lies in the reestablishment of moral codes and the return to the strict biblical injunctions of a clean life. To those who wish to save most eyes, there is one high road to success, prevent syphilis and gonorrhea. The day of smug secretiveness is past, birth control measures and contraceptives are known to all. Let us be more open in our condemnation. It is not sufficient for us to state the blunt facts of the woes that follow infection. The clergy and the lay organizations must shoulder the brunt of this battle.

Physicians have always told children of these dangers but rarely except in unusual cases have they really explained the dire effects which follow straying from the paths of righteousness. This subject is distasteful to many, but how much worse are the penalties of ignorance or perverseness?

The hygienic rules of life must be followed if we wish to maintain ocular health. Excessive indulgence in alcohol or tobacco, over-eating and over-work, especially mental, are reflected on the sensitive perceiving apparatus of the eye and may cause damage to the optic nerve or retina.

Unscrupulous purveyors of drugs and mechanical appliances fatten on cataract cases. There are few places where the faker finds more gullible individuals than among those suffering from the slowly progressing forms of cataract. When you consider that some cataracts may progress so slowly that even when re-examined at ten-year periods the advance is so slight as to be hardly perceptible, you will appreciate the fruitfulness of this field. When the untrustworthy, the uninformed or the untruthful say that they are controlling or stopping the progress of cataracts by any known method, I am skeptical. I wish to have you thoroughly understand the chronicity of the process and particularly that a lens opacity may reach a certain stage and then show no progression for years, and again I tell you that there are no drugs, no treatments or no devices which have altered the progress of any senile cataract. If anyone wishes to controvert this statement all I ask him to do is present properly controlled cases to prove his statements. Therefore, don't delude yourselves, don't mislead patients and don't urge friends to undergo expensive, time consuming treatments the results of which are valueless.

When a cataract has reached a certain stage of growth, and this does not mean that the sufferer has become blind, an operation will in most cases restore sight. There is so much talk about special cataract procedures that a layman is confused when it comes to the selection of an ophthalmic surgeon. The operator must use the method which is best for him and the one that gives the greatest promise of a

successful outcome. Anyone who has followed a cataract case understands that after the eye has healed glasses are worn to take the place of the lens, the cataract, which was removed. The extraction of a cataract is one of the most beneficial of all operations, for the patient is taken from darkness and brought into light.

You recall that we said the diagnosis of glaucoma was a very technical procedure. The treatment of the disease calls for unusual knowledge. The patient suffering from primary acute glaucoma must be operated upon if the sight is to be restored. The procedure of choice is an iridectomy, a removal of a piece of the colored portion of the eye.

Simple non-congestive glaucoma may under certain conditions be controlled by the use of miotics, drugs which contract the pupil. When, however, it is noted that the field of vision is contracting, the elevated intraocular tension unaltered, and the ophthalmoscopic changes more manifest, then an operation is necessary. The object of the mechanical interference is to permanently reduce the excessive intraocular pressure. A great many operations have been proposed and performed. Unfortunately, the results are not all that we wish. The sufferer with glaucoma must be cooperative and willing to do whatever his physician considers best. He should know something about the clinical course of glaucoma, he must continue to use his eyes, be taught to maintain an hopeful outlook and appreciate that at any time the disease may be controlled and some vision maintained for life.

When blindness threatens the patient with hypertension, arteriosclerosis and other constitutional diseases, he must be under the combined supervision of the internist and ophthalmologist.

The treatment of tuberculosis of the eye follows the rules accepted for the care of the pulmonary invasion. The use of the eyes is strictly regulated and in suitable cases tuberculin administered.

There are few conditions more distressing than detachment of the retina. Innumerable methods of treatment have been proposed and followed for its relief but, unfortunately, the results have been disappointing. During the past few years new hope has been given to the sufferer of detachment by the more universal acceptance and application of present-day knowledge regarding the disease process. The patient is placed in appropriate surroundings and after very technical and repeated examinations, the rent in the separated portion of the retina is outlined and then by means of chemicals, galvano-cautery or high frequency electric currents, the surgeon attempts to seal the opening and reattach the retina to its former base. The latest form of treatment, diathermy, seems to be the one on which most of us now depend. The operation is done under a local anaesthetic and the patient remains quiet in bed for several weeks. In the favorable case the retina is replaced and sight restored. This newest operation has not received the widespread publicity which it deserves. Time plays an important part in the restoration of vision for if the retina has been separated from the choroid for too long a period, even if the mechanical replacement is secured, function is not restored. We may confidently expect that more patients with a detachment of the retina will present themselves for an early operation when they learn of this improvement in technical results.

When a cancer is found in an eye, the eyeball should be enucleated. There are very few exceptions to this rule, one is in bilateral glioma where radium may be tried. A few cases have been successfully controlled by its use.

The neurologist by means of the ocular symptoms and signs is able to localize brain diseases; meningitis, tumors or abscesses. The intraocular end of the optic nerve is such a delicate indicator of pressure and inflammation that much confusion still exists in diagnosing the former from the latter. Fortunately, modern stereoscopic fundus photography offers a most accurate method of differentiation for by the pictures the earliest signs of obscure intracranial diseases are often quickly and correctly interpreted. When

we examine the domain of brain surgery, we are amazed at the skill and daring of the intrepid workers in this field. Never in the history of mankind has there been such a chance of preserving or restoring sight endangered by brain pressure. The marvelous progress of this superb endeavor is evidenced every day. When the optic nerves or tracts are compressed by tumors or by pus collections, their integrity is threatened and an operation becomes imperative.

The lesions of multiple sclerosis may simulate the retrobulbar change which results from nasal sinus infection, diabetes and chemical poisons, including alcohol and tobacco. The diagnostic skill of the physician is sometimes taxed to decide which is the causative factor.

To the trained ophthalmologist this summary may be uninteresting, to the non-medical members of the groups engaged in the prevention of blindness the citations should appeal for they form the basis of our arguments for relief.

When we consider all of the possible causes of poor vision, there should be no difficulty in arousing the interest of everyone in a more intensive campaign for the prevention of blindness. The scope of such a movement would be boundless, the opportunities for service unlimited and the rewards soul-satisfying. The task would be stupendous for the ramifications of disease lead us into countless embarrassments and the ways of prevention are infinite.

The members of the medical profession are keenly alive to their obligations and responsibilities, they are willing and anxious to initiate and carry forward plans for the early recognition of the potential causes of poor vision, expand their present organizations and cooperate with worthwhile established agencies. They are not willing to be further exploited or dictated to by their inferiors in understanding and skill. They object to local guilds or local blind worker groups assuming the power to select physicians to care for sick eyes.

We trust that those who have a deep interest in the prevention of any disease will understand this commendable

attitude of the sincere physician and cease to irritate him by assuming unwarranted dictatorial powers.

The ophthalmological sections of our State and National Associations and our special eye societies lead the way to ocular health. Those who wish to do most to prevent blindness should enter into a closer union with them. The astute leaders of medicine and the dictators of lay and legal associations are cognizant of the needs.

When we investigate the agencies working in the preventive field, we promptly acknowledge the achievements of the State Departments of Education, who by their almost universal system of school inspection occupy the most strategic and strongest position for the early recognition of visual defects. The State Departments of Health by their activities in the control of venereal infections stand high in the list of the important factors in the prevention of blindness.

The National Society for the Prevention of Blindness, a voluntary organization founded in 1915, has succeeded in doing a difficult task in an admirable way. It applies the facts advanced by physicians to alleviate the condition of the blind and prevent visual loss. The work of its successful administrators will always shine as a light in the field of darkness and as time passes a new, broader and more comprehensive program will be established to use the technical skill of more ophthalmologists, more obstetricians and more physicians. This will add greater luster and more brilliance to the Society's long record of achievements. The present director and his assistants merit our praise and approbation for their past accomplishments and our sincere good wishes for the future.

The Departments of Labor and Compensation have aided materially in improving the condition of the worker and we commend their efforts. The State Commissions for the Blind can do much more and better work if they, like others, accept organized medicine as an equal partner. Lastly, we speak of the local associations which combine prevention with care for the economic conditions of those

already blind. Their usefulness will be increased if they follow the suggestions of medical men.

In conclusion, let us seriously ask, "Where does my unit fit into the complicated scheme of a cooperative, unified, efficient Prevention of Blindness program?" And then let us triumphantly advance under the bright flag of hope which bears upon its silken folds the words, "Under inspired medical and trained social leadership all forces combine to conquer the causes of blindness."

A NOTE ON NARCOTICS IN ANCIENT GREECE AND IN ANCIENT CHINA[1]

EDWARD H. HUME

I. *Narcotics in the Odyssey.*

The word φαρμακου occurs in the Odyssey sixteen times. In the passage quoted below it signifies a remedial, sedative or narcotic drug. In other passages it refers either to a poison, smeared on arrows or mixed with food; or to a magic or enchanted drug. The passage quoted occurs in the fourth book of the Odyssey, lines 219 to 230 inclusive; the scene is in the palace of Menelaos at Sparta, years after the sack of Ilium. Telemachos, son of Odysseus, and Peisistratos, son of Nestor, have set out from Ithaca to find Odysseus if he be still alive, and have come to inquire of Menelaos and Helen. It is at the close of the day, and all are weary:

"Then Helen, born of Zeus, planned otherwise. Straightway into the wine of which they were drinking she cast a drug to assuage suffering and to dispel anger, and to cause forgetfulness of all ills. Whosoever should drink this down, when mingled in the bowl, would not, in the course of that day, let a tear fall down over his cheeks; not even if, before his face, his brother or his beloved son they should slay with the sword, and with his own eyes he should behold it. Such cunning drugs had the daughter of Zeus, potent drugs, which Polydamna, the wife of Thor, had given her; a woman of Egypt, for there the ploughed earth, giver of food, bears greatest store of drugs; many that are potent when mixed and many that are baneful.[2]"

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[1] Read at the Meeting of the Section of Historical and Cultural Medicine November 1, 1933.

[2] Modified from the translation by A. T. Murray in the Loeb Classical Library.

II. *Narcotics as Used by Pien Ch'iao and Hua T'o of China.*

1. *Pien Ch'iao.*

In Volume 105 of the *Annals of History*, a great Chinese classic, there occurs a long biographical note about Pien Ch'iao, a physician of distinction who lived about 255 B.C., in the city of Cheng in the prefecture of P'u Hai (possibly in the modern province of Honan). No name stands higher than his in the annals of Chinese medicine, and the honor paid to him is wholly comparable to that which the Western World pays to the memory of Hippocrates. The passage quoted is found in the writings of Lieh Tze, a later historian (Lieh Tze T'ang Wen P'ien).

"Two men, Lu Kung-hu and Chao Ch'i-ying, fell ill and came together to seek treatment from Pien Ch'iao. After treating them, when both were recovered, he said, calling them by name, " The illness from which you suffered previously came to your organs from external influences and was susceptible to medical treatment. You now have a malady which attacks both of you together. Do you wish it treated?" Both men asked that he first give them the results of his examination.

Pien Ch'iao addressed Kung Hu and said, "Your will is strong but your spirit is weak; hence you are strong in one respect and weak in another. The will of Ch'i Ying is weak, but his spirit is strong. If your hearts were exchanged, there would be an equilibrium and the result would be good."

So then Pien Ch'iao caused the two men to drink a drugged wine, which made them insensible, as if dead, for three days. He cut open their chests, investigated and exchanged their hearts and replaced them, employing potent drugs. When they recovered consciousness, both men were as at the first, took their leave and went home.*"

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* Modified from the translation by E. Faber.

stitute for opium. The Sanskrit word is *bhanga*. "The Persian word is also traced to Avestan *banha*, a narcotic, but it seems to me preferable to assume direct derivation from Sanskrit in historical times."

Other drugs used for their narcotic effect include the following:

1. *Aconitum fischeri*. (In Europe, "monk's hood" or "wolf's bane"). The Chinese name is *Wu t'ou*, a plant used at least as far back as the end of the third century A.D. by the physician Ko P'u. Large quantities are shipped down the Yangtze River from Szechuan. The Sanskrit term is *visha*, probably *Aconitum ferox*.

2. *Arum pentaphyllum* and *Arum triphyllum*. The Chinese generic name is *Hu chang*. This plant was known to the Greeks as αρου. In England it is commonly called "cuckoo-pint" or "wake-robin."

3. *Datura alba*. In 1662, J. Davies, translating "Mandeslo's Travels" said, "The Indians call this drug *dontro* or *datula*. It is a drug that stupefies the senses. The Turks and Persians call it *datula*." Two species are described in India, *Datura fastuosa* and *Datura metel*; in Western Asia a species exists known as *Datura stramonium*, or the common thorn-apple. The drug is said to stupefy and poison. The Marathi name is *Dhatura*, while the Sanskrit uses both *Matula* and *Dhatula*. The Chinese have a drug which stupefies, called *Mant'o lo hua*, which is evidently a transcription from the Sanskrit *Matula*. The Encyclopedia of Pharmacals identifies it, however, as *Lycium chinense*.

The plant definitely identified as *Datura alba* is *Nao yang hua*, "the flower that makes sheep dizzy." Some identify this plant with *Hyoscyamus niger*.

4. *Hyoscyamus niger* (Henbane). Laufer (*loc. cit.*) makes it clear that *bang* in Persian refers to *Hyoscyamus*, but that the word is derived from the Sanskrit *bhanga*, which is *Cannabis sativa*.

Further researches, historical, botanical and pharmacological, are needed before there can be more complete identification of the narcotics used by ancient Chinese surgeons.

REPORT OF THE COUNCIL
CHARGES AGAINST DR. FRED H. ALBEE

The Council at its meeting held on May 23, 1934, adopted the following resolutions:

"RESOLVED, That the Council herewith charges Dr. Fred H. Albee as follows:

"1. That he furnished information and material for the purpose of publicity to Mr. S. B. Murdock, General Passenger Agent of the Seaboard Air Line Railway Company which resulted in the printing on the menus used in the dining cars of that Company, and on hand bills distributed in the streets of St. Petersburg and Miami, Florida, in the fall of 1933, of such information and material which constituted a form of advertising of such character as to invite attention to himself and his professional position and connections.

"2. That such action of Dr. Albee unfavorably affects the character of the medical profession and the interests and reputation of the Academy.

"3. That he failed to take effective action to stop such advertising after it had been brought to his attention.

"RESOLVED, That the Council hold a hearing in accordance with the provisions of Article IX, Section 9, of the By-Laws of the Academy on June 19, 1934, at 4 o'clock in the Council Room of the Academy of Medicine, 2 East 103rd Street, in the City of New York, at which the foregoing resolution shall be read to Dr. Albee and he shall be given full opportunity to make such statement as he may wish with regard to the charges therein contained and may have such witnesses testify in his behalf as he shall desire.

"RESOLVED, That the Secretary of the Academy be and hereby is authorized and instructed to send a certified copy of the foregoing resolutions to Dr. Albee."

A certified copy of these resolutions was sent to Dr. Albee who appeared with counsel at the special meeting of the Council held June 19, 1934.

At an adjourned meeting held June 26, 1934, the Council by unanimous vote found Dr. Albee guilty on all of the charges, and the Council, acting under the authority conferred upon it by the Constitution and By-Laws of the Academy, suspended Dr. Albee from The New York Academy of Medicine for a period of one year from June 26, 1934.

BACK NUMBER OF THE MONTHLY BULLETIN WANTED

Fellows of the Academy who can spare copies of the June, 1934, number of the Bulletin are requested to send them to the Assistant Secretary at the Academy.

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London, Milford, 1934, 212 p.
Wroth, L. C. An American bookshelf, 1755.
Phil., Univ. of Penn. Press, 1934, 191 p.

DEATHS OF FELLOWS OF THE ACADEMY

Allen, Thomas Herbert, M.D., Mahopac, New York; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1875; elected a Fellow of the Academy January 6, 1881; died September 22, 1934. Dr. Allen was a member of the County and State Medical Societies and a Fellow of the American Medical Association. He was consulting physician to City Hospital.

Davis, Fellowes, Jr., M.D., 5 Place Vendome, Paris, France; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1899; elected a Fellow of the Academy May 15, 1913; died, September 5, 1934. Dr. Davis was a member of the surgical staff of New York Hospital from 1904 to 1914, and attending obstetrician to the New York Nursery and Child's Hospital from 1911 to 1921.

Easton, Charles Daniel, M.D., 510 Park Avenue, New York City; graduated in medicine from Harvard Medical School in 1904; elected a Fellow of the Academy April 1, 1926; died, October 4, 1934. Dr. Easton was a member of the County and State Medical Societies and a Fellow of the American Medical Association. At the time of his death he was physician to Newport Hospital, Newport, Rhode Island.

Fuchsius, John Hancock, M.D., 151 Centre Avenue, New Rochelle, New York; graduated in medicine from Bellevue Hospital Medical College, New York City, in 1899; elected a Fellow of the Academy January 4, 1912; died, September 5, 1934. Dr. Fuchsius was a Fellow of the American Medical Association and a member of the County and State Medical Societies. For a

number of years he was associated with the Manhattan Eye, Ear and Throat Hospital, Harlem Hospital and Post-Graduate Hospital in New York City and for twenty-six years with the New Rochelle Hospital in the ear, nose and throat department.

SATTERTHWAITE, THOMAS EDWARD, B.A., M.D., LL.D., 7 East 80 Street, New York City; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1867; elected a Fellow of the Academy May 4, 1882; died, September 19, 1934. Dr. Satterthwaite was a former president of the New York Pathological Society, of the American Therapeutic Society and of the Medical Society of Greater New York. He was one of the founders of Babies' Hospital and its President from 1894 to 1899, and of the Post-Graduate Medical School at which he was Professor of Pathological Anatomy and Internal Medicine. For 10 years he was on the staff of St. Luke's Hospital, for 15 years Pathologist to Presbyterian Hospital, and was consulting physician to Post-Graduate, Orthopedic and Manhattan State Hospitals. He was a frequent contributor to medical literature.

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EDITORIAL

HISTORY OF GASTRO-ENTEROLOGY

(With Special Reference to American Developments)[1]

From the time of Beaumont to the present, the physiology, pathology and surgery of the digestive tract have been not a little indebted to American enterprise and invention. In Germany, Kussmaul (1869), Leube, Ewald and Boas were the prime movers of recent developments. Boas was the first to specialize in gastro-intestinal disorders alone (1886), indeed started the first clinic and founded the first periodical (1896). The American Gastro-Enterological Association was founded in 1897, the German organization in 1914. Thus, a certain number of practitioners have been following gastro-enterology as a specialty for nearly half a century. Both Frerichs and Nothnagel stressed the backward condition of the subject in their time. Expansion was comparatively late, and mainly Germanic and American. This development had a long foreground and only the bare outlines of its history are known.

The interdictions put upon unsuitable, unclean or poisonous foods in the Mosaic code (Exodus, Leviticus) go back to the initial experiments of prehistoric man with regard to things edible or inedible. Everything was tried; much was learned from the avoidances of birds and animals; but

1. Read at the one hundredth meeting of the New York Gastro-Enterological Association, Union Club, October 11, 1934.

was necessarily obscure. Anorexia, excessive appetite (*bulimia*), excessive thirst (*polydipsia*), nausea and vomiting, sea-sickness and hiccough were all classified primarily as œsophageal disorders, yet recognized as symptomatic of gastritis and other digestive ailments. Diseases of the spleen and of the portal vein were long associated with the digestive system. Gastritis and hepatitis were recognized as such and handled at length, in separate chapters, by Aretaeus, Celsus and Alexander. Hepatitis might merge into jaundice, hepatic abscess or cirrhosis. The coeliac passion (*morbus coeliacus*) was a foul diarrhœa, associated with chill or atony of the stomach. Stools were sometimes examined in such conditions. The iliac passion (*ileus, volvulus, chordapsus*) was intestinal obstruction, often confused, for many centuries, with appendicitis. Diarrhœa, cholera, dysentery, ileus and painful stools (*tenesmus*) were allocated to the intestines. Colic was allocated to the colon. Intestinal ulcers were known. In the reading of Aretaeus, lientery (ridiculed in Molière) was a cachexia, usually associated with intestinal adhesions. Hippocrates and Aretaeus left masterly pictures of cholera, dysentery, jaundice and ileus. Alexander Trallianus notes three classes of intestinal parasites, viz., the thin, small worms causing anal pruritus (*Oxyuris vermicularis*); the round worms in the upper bowel (*Ascaris lumbricoides*); and the long flat worms, which often occupied the entire intestinal tract (*Taenia*). Pomegranate juice, male fern, castor oil, hellebore and thyme were employed as vermifuges. The test of expulsion that of the young lady in Charles Reade's novel: "I see the vermifuge has acted." In the Alexandrian period, Erasistratus had already devised a rude calorimeter.

For centuries, the theory and practice of digestion and its disorders was under the sway of the humoral pathology, in other words, virtually at a standstill. Beyond the dietetic precepts in the *Regimen* of the School of Salerno (1260), little was added to the practical knowledge accumulated by the Greek physicians. Associated with the four humors and the doctrine of planetary influences was the mediæval theory of the constitution, centering in the four temperaments, viz., the sanguine (Jovial), choleric (Martial), phlegmatic (Mercurial) and melancholic (Saturnine). The bilious or cholæmic diathesis, attributing jaundice to yellow e and a dour disposition to black bile, became basic in ic and tropical pathology, even down to the days of eppery nabobs of the Anglo-Indian service. How little s added to the anatomy of the digestive tract before Leonardo and Vesalius is suggested by the terminology employed by Shakespeare and his fellow dramatists. In

keeping with Greek and Roman usage, the stomach (*ventriculus*) was equated with the belly (*venter*), as in the parable about the belly and the members in Coriolanus (I, 1) or the episodes of Falstaff and Justice Greedy (Massinger). Up to very recent days, the "fair, round belly with good capon lined" was regarded as a natural attribute of the elderly, who now obliterate the semblance of a swallowed watermelon by dint of golfing and banting. As depicted by Athenaeus, the Elizabethans and later writers, the capacity of the ancients, the English, the Germans and the Russians for food and drink seems beyond human credibility. Gluttony was early ridiculed in the bursting belly of Philoxenus (Athenaeus, viii, 341), which was plagiarized by La Fontaine (*Le Glouton*) and later by Pope:

> "The doctor call'd, declares all help too late:
> Mercy, cries Helluo, mercy on my soul!
> Is there no hope?—Alas!—then bring the jowl."

The drinking song in Gammer Gurton's Needle (1575) begins:

> "I cannot eat but little meat
> My stomach is not good,"

but a minute later, we have the reason, in the shape of a resounding chorus:

> "Back and side go bare, go bare,
> Both foot and hand go cold,
> But belly, God send thee good ale enough,
> Whether it be new or old."

There was manifest wisdom in the saw of the Persian poet Saadi that an empty belly connotes mental and spiritual activity or *vice versa;* whence the stomach, sometimes the whole gastrointestinal tract, became associated with pluck and courage ("guts"); fighting capacity with a full stomach ("Armies travel on their bellies") and the intestines, in particular, with compassion. Thus Wicliffe (1332) refers to the "bowels of Jhesu Christ," Sir Thomas Browne (1642) to "bowels of pity" (*Religio Medici*) and Jeremy Taylor to the "bowelless hangman" (1649). Even in Bulwer's Eugene Aram (1832), we read: I am a man that

can feel for his neighbors. I have bowels. I have bowels." The colon was sometimes equated with the stomach, e.g., "to feed colon" (Massinger, *Virgin Martyr,* III, 3) or Heywood's "What trick to satisfy colon?" The liver, for long regarded as the factory of the blood and one of the twin motors in the Galenic scheme of the circulation, was associated with courage, a touchy disposition and amorous propensities. Thus Hamlet (II, 2): "I am pigeon-livered and lack gall," or Chapman's "my venerean gentleman's hot liver" (*Widow's Tears,* 1612) or "I am all liver and turned lover," in an old play of 1606. The ancient fear attaching to a diseased liver in sacrifice and divination is reflected by Cassandra in *Troilus and Cressida* (V, 3):

> "Polluted offerings more abhorred
> Than spotted livers in the sacrifice."

Milton, Evelyn and Smollett describe a victim of congested liver as "liver-grown." Such expressions as "to stomach insults," "digest your angry choler" (*King Henry* VI, iv, 1), or to "digest the venom of your spleen" (*Julius Caesar,* IV, 3) are plainly survivals of an archaic physiology. In two places, Shakespeare maintains the old Galenic functional tripod of the heart, the liver and the brain (*Cymbeline,* V, 5; *Twelfth Night,* I, 1).

Up to the time of Beaumont, the physiology of gastric digestion was obfuscated by a series of dissolving views, summarized in William Hunter's epigram that the stomach was variously regarded as a mill, a fermenting wine-vat or a stew-pan.

To Galen, digestion was coction; in virtue of which, the stomach extracts what it needs from ingested food and passes on the rest to the intestines, the liver and other parts of the body *viâ* the blood channels. The mechanical view was advanced by Borelli and the Iatro-physicists, who limited gastric digestion to the grinding and crushing action of the musculature of the stomach. Baglivi even likened the teeth to scissors, the glands and viscera to sieves. The Iatrochemical theory of digestion as chemical fermentation was largely the work of Van Helmont, who maintained the old Galenic view that the products of digestion acquire natural spirits in the liver, which become vital spirits in the heart and animal spirits in the brain. Digestion is a continuous fermentative process in six stages. The acid, chyle-forming ferment in the stomach derives from the spleen. In the last stage, the tissues

and organs absorbing the blood charged with vital spirits are envisaged as "kitchens." The stomach itself is the seat of the soul, since a knock-out blow at the solar plexus may destroy consciousness. The pancreatic duct was discovered by Wirsung (1642), the submaxillary duct by Wharton (1655), the parotid duct by Stensen (1661). Sylvius, therefore, stressed the rôle of the saliva, regarded both gastric and pancreatic juices as acid and may be credited with some vague notion of acidosis. De Graaf obtained saliva, bile and pancreatic juice from the dog by canalising the parotid, biliary and pancreatic ducts (1664). His work seems prophetic of Beaumont, as Brunner's experimental excision of the pancreas (1683) seems prophetic of Banting. Réaumur obtained gastric juice from the stomach of kites and demonstrated its solvent action upon foods outside the body (1752). Spallanzani confirmed those findings but denied that the solvent principle is an acid (1782). Young of Maryland proved what Van Helmont and Sylvius had surmised, that the gastric juice contains an acid, turning litmus paper red (1803). This acid Prout showed to be HCl (1824). Through an accidental window in the stomach, Beaumont, a year later, was able to view and describe the processes of gastric digestion and gastritis *in situ* (1825), noted the inhibition of digestion by emotion, constructed a dietetic table from the digestibility of different foods and thus created the true physiology of gastric digestion (1833). Gmelin and Tiedemann discovered tryptophan (1826), which Claude Bernard subsequently proved to be a by-product of pancreatic digestion. The Gmelin test for bile (1826) had been anticipated by Marabelli (1788). Purkinje and Pappenheim noted the proteolytic power of the pancreatic juice (1836) and Lucien Corvisart that this solvent action is independent of acidity or alkalinity (1857-63). Claude Bernard revived the experimental pancreatic fistula of De Graaf and demonstrated the rôle of the gastric juice in emulsifying fats, changing starches into sugar and dissolving the proteins passed on to the intestines from the stomach (1849-56). The conversion of proteins into peptones within the stomach was first described by Meissner (1859-62). Ptyalin was discovered and isolated by Mialhe (1845), trypsin by Willy Kühne (1876), biliverdin by Berzelius (1840); bilirubin by Heintz (1851); urobilin by Max Jaffé (1859).

Magendie first described the mechanisms of vomiting (1813) and deglutition (1817) but missed their reflex character, which was later elucidated by Kronecker and Meltzer (1880-83). Beaumont's observations on the movements of the stomach were confirmed in an excised preparation by Hofmeister and Schütz (1886), but the real elucidation of this matter came from W. B. Cannon, who, at the instance of Bowditch, employed the x-rays (1896-1902). His findings are summarized in his book on The Mechanical Factors of Digestion (1911).

Cannon was the first to elucidate the mechanisms of gastrointestinal digestion with x-rays and the bismuth (eventually barium) meal. He

showed that the peristaltic wave travels continuously to the pylorus, with some slowing in the rate of conduction at the bridge, that the pylorus has an autonomy of its own in passing food on to the duodenum; that the pendulum movements of the small intestine (Ludwig, 1861) resolve themselves into rhythmic segmentations, to mix the content with the intestinal juices, culminating in a terminal peristaltic rush to the lower bowel; that the colon employs reverse peristalsis in the condensation of fæces and that the whole peristaltic process is affected by anæsthesia, surgical intervention, illness or other factors. Reverse peristalsis, contested by Mall, is a property of the entire gastrointestinal tract. In 1912-13, Roger Glenard illustrated intestinal peristalsis, particularly during purgation, by the cinematograph. Alvarez, by means of moving pictures of the exposed digestive tube, has elucidated Cannon's findings in great detail, particularly *re* the doctrine of gradients (1914-18). Carlson has investigated in detail the hunger contractions of Morat (1882) and Boldyreff (1904-14), showing functional activity even in the fasting stomach, which becomes very painful in the cases of gastric ulcers. The net result of these findings is to the effect that the gastrointestinal tract, like the heart, is an autonomic motor mechanism, which can function by the rhythmic, cell-to-cell transmission of impulse by the muscular tracts alone, even when excised from the body, and in which the nerve supply and intrinsic ganglia act as centralizers and coordinators in expediting conduction. Alvarez likens the coordinating nervous mechanism to a telegraphic or telephonic system attached to a railway or a factory, which can nevertheless run of themselves on occasion. The neurogenic theory of motor activity, which Magnus set out to prove in the intestinal musculature, has been completely supplanted by the myogenic.

Pavloff did for the secretory activities of digestion what Cannon did for the motor mechanisms of the gastro-intestinal tract. His work covers the whole broad field of the effect of emotion upon digestion, merging logically into the doctrine of conditional reflexes and behaviorism.

Psychic secretion of gastric juice had been noticed in a gastrostomized dog by Bidder and Schmidt (1852) and in man by Richet (1878). But by combining the improved Heidenhain fistula with an œsophagotomy, Pavloff and his pupils were able to cover all aspects of sham meals and psychic secretions. Secretin, the intestinal hormone which activates pancreatic secretion, was postulated by Bayless and Starling (1902); enterokinase by Pavloff (1899). The bile-forming function of the liver was known to the ancients. In the Galenic view, the undigested material carried from the stomach and the intestines to the liver by the gross blood in the portal vein was converted into pure blood by the separation of yellow bile (carried to the gall-bladder) and black bile passing to the spleen. The glycogenic function of the liver was discovered by Claude Bernard (1843-57). That the formation of bilirubin is associated with the disintegration of hæmatogen was known to Stadelmann (1890), Minkowski, Naunyn and others.

In 1913, Whipple demonstrated the possibility of extrahepatic formation of bile by excluding the liver *viâ* an Eck fistula. Mann proved this conclusively by excision of the liver (1924-5), showing that bile can be formed by histiocytes in the spleen, bone-marrow and connective tissue. This, one of the greatest discoveries in the history of physiology, is associated with the functions of the reticulo-endothelial system and the subsequent discovery of the treatment of pernicious anæmia by raw liver (1925-6). The metabolic relations of the liver and the other digestive organs is matter of vast extent.

Up to the 19th century, little of consequence was added to the knowledge of digestive disorders outlined by the Greek physicians. The most suggestive approach, the pediatric, was totally neglected, although the prevention of gastrointestinal disturbances in infancy, by breast-feeding, selection of proper wet-nurses and milk-tests, was well developed among the Greeks and the ancient Hindus.

The meconium was voided by placing a little honey upon the lips of the new-born (the sugar diarrhœa of Orgler). This practice continued up to the Middle Ages, when a bit of sugar or sugared baked-apple was substituted. In the 17th century, Walter Harris, a pupil of Sydenham, adumbrated the doctrine of acidosis in infancy, which he treated by chalk and pearl juleps. Apart from gout and dysentery, Sydenham himself has little to say of digestive disorders in the adult. Jan Heurne, memorable for his association with the beginnings of bedside teaching, left a posthumous pamphlet on diseases of the stomach (1610); Ferriol, a little book (1668). Martin Harmes wrote on diseases of the stomach and intestines (1684). A favorite theme of the 17th century physicians was the dyspepsia from gastric atony implicit in the title "*De imbecilitate ventriculi.*" This usage continued into the 18th century, when it was sometimes equated with the "hectic stomach" (Arnold, 1743) and later with the *embarras gastrique* of the French clinicians. Swalbe (1664) published a lengthy satire on "the quarrels and opprobria of the stomach" (*prosopopoia*). A more varied spirit of observation was manifested, here and there, by the 18th century physicians. In 1723, Boerhaave described a famous case of rupture of the œsophagus (autopsy on Baron Wassenaer, Pohl wrote on hardening of the stomach from abuse of alcohol (1771), Mertlick on intestinal sand (1786), Vanos (1704) and Lobé (1788) on diseases originating from gastric disorder. Congenital pyloric stenosis was described by Patrick Blair (1730), George Armstrong (1777) and, in America, by Hezekiah Beardsley (1788). Only two additional cases were recorded before 1888. Reil established the concept "polycholia" in 1782. Cowley had some notion of pancreatic diabetes in 1788. The literature on

dyspepsia is large. The old doctrine of acidity (*De humore acido a cibo orto*) is reflected in Joseph Black's dissertation on CO_2 (1754). Friedrich Hoffmann published a long series of tracts on gastric hæmorrhage (1679), saliva (1693-4) and its examination (1698), *Pumpernickel* (1695), apepsia (1696), diarrhœa in acute diseases (1700), gastritis (1706), diseases of the duodenum (1708) and the pancreas (1713), oatmeal cure (1714), iliac passion (1716), hepatitis (1721), diseases of the œsophagus (1722), cancer of the liver (1722), emesis (1725), pathology of liver diseases (1726), blood vomiting (1729), pharyngeal spasm (1733) and nausea (1733), which, if assembled, would make a very respectable manual of digestive disorders.

No such range of versatility in observation is apparent in any text-book between Hoffmann's period and that of Austin Flint (1868). The contents of early treatises on practice include no more than the diseases handled by the ancient writers, viz., dyspepsia, constipation, diarrhœa, colic, gastritis, enteritis, ileus, intestinal worms, jaundice, hepatitis and sometimes cancer of the stomach. A respectable fourth of Flint's Practice is taken up with digestive disorders and from this time on through the rest of the 19th century, there is farther expansion.

Among the earlier English books are those of Stone (1806), Marshall Hall (1820), Hare (1821) and Abercrombie (1828) on digestive disorders, Armstrong's pathological atlas of digestive diseases (1828), Rees on diseases of the stomach (1810), Howship on intestinal diseases (1820), Gibson (1801), William White (1808) and Faithorn (1814) on liver complaints. Later came George Budd's classics on diseases of the liver (1845) and stomach (1855), Brunton on diseases of the stomach (1859), which contains his account of plastic linitis, Frerichs (1858) and Murchison on liver diseases (1868). Contributions of enduring value were those of Laennec (1819), Hayem (1874) and Hanot (1876) on cirrhosis of the liver, Cruveilhier on the pathology of the peptic ulcer (1835), or Rokitansky's account of the pathology of acute yellow atrophy (1843) which Morgagni had described in 1762.

During 1867-9, Kussmaul began to employ the stomach tubes in the treatment of gastric dilatation and with this innovation, the modern development of gastro-enterology began. While stomach-pumps had been invented and employed by Alexander Monro (1767), John Hunter (1790) and Physick (1812) in the treatment of poisoning, this was a new departure. In 1871, Leube began to use the stomach-pump for diagnostic purposes, to experiment with test-meals and to envisage the concept "nervous indigestion," which was developed by Rejchmann (1883). Oser intro-

duced the flexible tube, which Ewald put into practice in 1875, combining aspiration of the gastric contents, with Boas' device of expression. Ewald and Boas then made test-meals viable. Ewald's Clinic of Digestive Disorders was published in 1879-88. Boas opened the first clinic (1886), began to lecture in the subject and published his text-book on diseases of the stomach in 1890-93. According to Bassler, he devised the resorcinol test, postulated the Boas-Oppler bacillus and the lactic acid and the high frequency of bleeding (95 per cent) in gastric cancer and used the test-supper to estimate gastric motility. Nothnagel's classic on diseases of the intestines and the peritoneum was published in 1896. From this time on, progress was rapid.

Mikulicz introduced gastroscopy and œsophagoscopy (1881). Glénard introduced diagnostic improvements (1885) and described the visceral ptoses (1887). Hirschsprung described megacolon (1887) first noted by William Leavitt (Chicago) in 1867. Bard and Pic described primitive cancer of the pancreas (1888) and Fitz hæmorrhagic pancreatic necrosis (1889). Sahli is memorable for advances in diagnosis. Knowledge of jaundice and its modalities was forwarded by Weil (1888), Stadelmann (1891), Chauffard (1907), Widal (1907), McNee (1913-14), Inada and Ito (1916) and others; diseases of the pancreas and pancreatic diabetes by Mering and Minkowski (1889-93), Opie (1901-3); Ssoboleff (1902), Cammidge (1904); MacCallum (1909), Banting and Best (1924); biliary calculus by Naunyn (1892) and Aschoff (1909). The Plaut-Vincent angina (trench-mouth) was established in 1894-6.

Much light was shed by visceral surgery, which Naunyn described as an "autopsy *in vivo.*"

Intestinal anastomosis, first attempted by the Salernitan surgeons, was brought to a high point of perfection by Abbe, Dean, Murphy, Halsted and Carrel. Billroth covered most of the alimentary tract through his resections of the œsophagus (1872), the pylorus (1881) and the intestines (1878-83). His pupil, Wölfler, introduced gastro-enterostomy (1881). In 1897, complete excisions of the stomach were done by Schlatter and by Baldy (United States). Lane's operation for intestinal stasis came in 1903. Marion Sims (1878) and Langenbuch (1882) excised the gall-bladder. Maydl introduced colostomy (1888) and Kraske resection of the rectum (1892). Appendicitis, known to the mediæval surgeons as *passio iliaca,* was early noted by Fernel, Heister and others; first operated by Mestivier (1759); accurately described by Fitz (1886) and standardized as to diagnosis and operative procedure by McBurney (1889). Subsequent operating on the gastro-intestinal tract by the Mayos, Weir, Deaver, Sands, Finney and other recent American surgeons

has been brilliant. From the time of De Graaf, the physiology of digestion has been materially forwarded by surgical intervention on animals. Success in this field was naturally hampered by ignorance of the comparative anatomy and physiology of animals in the earlier centuries. Laterly, such procedures as Sander's device of exposing the intestines under salt solution for study of peristalsis (1871), the Eck fistula (1877), Pavloff's flap modification of the Heidenhain gastric fistula (1880) with intact nerve-supply (1900) or Mann's exclusion of the liver by excision (1921-5) have become essential and indispensible.

Röntgenography of the digestive tract owes much to the fluorescent screen and the Coolidge tube.

Holzknecht, Handek and Groedel made the first worthwhile serial x-ray pictures of the stomach in man (1909-12). A. F. Hurst advanced the radiography of constipation and defæcation (1908). Graham and Cole made x-ray study of the gall-bladder possible (1923-4). The sphincter of the common bile-duct (Oddi,1887) was discovered by Simon P. Gage (1879). Non-surgical aspiration of the gall-bladder, for diagnostic and therapeutic purposes, was introduced by Meltzer (1917) and Lyon (1919). Recent American work, at the Mayo Clinic and elsewhere, includes the investigations of Eggleston and Hatcher on the action of emetics and the mechanism of vomiting (1912-15), Case on intestinal stasis (1914-15), Alvarez on the mechanics of digestion and its clinical applications (1914-27), Ivy on gastric secretion (1920-25), Boyden, Mann and Higgins on the mechanism of evacuation of the gall-bladder (1924-6); Einhorn introduced gastro-diaphany (1887), stomach and duodenal buckets (1890-1908) and duodenal intubation (1909). Fractional intubation of the stomach was introduced by Rehfuss (1914); functional pancreatic tests by Boas, Cammidge (1912), Einhorn, McClure and Bassler; hepatic tests by Ehrlich (1886-1900), Van den Bergh (1918) and others. Dietetic schemes for gastric ulcer were started by Leube (1897) and improved by Lenhartz (1904), Lambert (1908) and Sippy (1915). The bacteriology of the intestinal canal is associated with the names of Eberth, Escherich, Alexander Schmidt, Herter, Shiga, Flexner, Chalmers and Bassler.

The first independent periodical on digestive disorders was the *Archiv für Verdauungskrankheiten* (1895-6), founded and edited by Boas. Two years later, the American Gastro-Enterological Association was organized (1897), largely through the efforts of Aaron of Detroit. In 1914, Bassler founded the first American periodical, the *American Journal of Gastro-Enterology*. A section of Gastro-Enterology and Proctology was established in the American Medical Association in 1917. The New York Gastro-Enterological Association was organized on April 30, 1915, the

National Society for the Advancement of Gastroenterology in 1934. In connection with these developments, chairs were established in the principal medical schools of New York for Einhorn, Nesbitt, Kemp, Bassler, Kantor, Andresen, Chace and other leaders; of whom Aaron (Detroit), White (Boston), Simon (New Orleans), Alvarez (Mayo Clinic), Smithies, Carlson and Portis (Chicago), Rehfuss and Lyon (Philadelphia, Harris (Birmingham), Gerry Morgan and Verbrycke (Washington) and Soper (St. Louis) have been outstanding elsewhere (Bassler). Col. Seale Harris was in charge of the Division of Gastro-Enterology of the Surgeon General's Office during the World War. More recently, the Medical Department of the U. S. Army has organized sections of gastro-enterology in all general hospitals. The principal American text-books have been those of Einhorn (1896-1905), Hemmeter (1896-1901), Kemp (1910), Bassler (1910-30), Aaron (1911-15), Lockwood (1913), Niles (1914), Stockton (1914), Lyon (1923), Hurst (1924), Kantor (1924), Crohn (1927), Rehfuss (1927), Kellogg (1931), Alvarez (1931), Morgan (1931) and Backstein (1932). As to disorders of infantile and adult metabolism, diseases of the blood and the nervous system, the dietetic treatment of all manner of clinical and surgical conditions, endocrinology and vitamin-therapy, the subject has immense ramifications, to which only passing reference can be made. In the light of these developments and of the work of Young, Beaumont, Fitz, Cannon, Mann, Whipple, Einhorn, Graham, Cole, Bassler, Alvarez and younger men, the record of American achievement in gastro-enterology seems far from contemptible.

During the long five-year famine, which followed the World War and the Russian Revolution, there was a gigantic turn-over of pathological conditions in Russia, which is of unique interest in connection with problems of food-economics, dietetics and gastro-enterology. Of old, the Russians were most liberal addicts of the pleasures of the table and, apart from communicable diseases, suffered mainly from disorders incident to repletion. There were

dinners in pre-war Leningrad which were voted the best in Europe. At the International Medical Congress in Moscow (1897), few American physicians were equal to the banquet in wait for them, after negotiating the very lavish *Sakouska* of *hors d'œuvres*. During the famine period (1919-23), this dietetic set-up was literally upset. The disorders due to repletion were displaced and supplanted by disorders incident to depletion. Constipation, obesity, gout, diabetes, alcoholism, appendicitis, gastritis and liver complaints disappeared and gave place to anæmia, peptic ulcers, visceral ptoses, noma, pyorrhœa alveolaris, flatulence, meteorism, acute enteritis, gastric cancer, neuropsychoses and neurasthenia merging into sexual impotence, with an appalling mortality from diseases of the heart and circulation. In the darkest period, cannibalism was not infrequent, and there are rumors of another immense wave of starvation in the Ukraine latterly. At intervals, similar conditions have confronted the famine-stricken populations of Ireland, India and Polynesia, of post-bellum Germany and Austria and those recently affected by the drought in our own Western areas. The famine-medals of the Middle Ages are tokens of distinct heuristic value. The immediate future of humanity will be largely bound up with economic problems, of which the relations of demand and supply in food-economics is one of the most outstanding. Facilities for transportation and administration, so essential to distribution of food-supplies of large cities and areas, have not been adequate to meet the problem of food-shortage. How intimately the medical profession is concerned with the economic problems of poverty, unemployment, food-shortage and starvation is suggested by the verse of Heine about the doctor whose sole prescription for an indigent patient was nourishing food and drink. From this point, our subject expands to the widest implications of the ancient saw, that man is and becomes what he eats (*Homo est quod est*).

It is probably from this association with the good things of life that gastro-enterologists, like the pediatrists, are a very genial set of men.

F. H. GARRISON.

SEVENTH ANNUAL GRADUATE FORTNIGHT
"Diseases of the Gastrointestinal Tract"
October 22 to November 2, 1934

The Wesley M. Carpenter Lecture

THE APPLIED PHYSIOLOGY OF THE GASTRO-INTESTINAL INNERVATION*

Certain Selected Topics

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The subject of this lecture was chosen because of its general applicability to the topic under consideration during this fortnight of study. In view of the time allotted to the lecture the subject matter has been selected and will be presented in synoptic style. The topics selected pertain primarily to disturbances of motor activities, since disturbances of motility more frequently cause symptoms than disturbances of secretory activity.

All portions of the gastro-intestinal tract are intimately correlated by extrinsic and intrinsic nervous mechanisms and humoral agencies. Thus, in many diseases of the gastro-intestinal tract, we must think of the tract as a functional unit, and not solely of the viscus in which an organic lesion or disease is located.

First, I should like to discuss briefly the relation of the cerebral cortex to the autonomic control of the digestive tract. I am especially interested in this subject because of its highly probable relationship to the etiology of "peptic" ulcer. I have had sufficient contact with "peptic" ulcer patients to realize the rather important role played by sustained anxiety and the associated unhygienic eating habits in the genesis of ulcer.

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* Delivered October 23. 1934.

One of the most interesting developments in modern physiology has been the demonstration by Pavlov that, as a result of a learning or conditioning process, a non-instinctive stimulus may excite or inhibit the gastric or salivary glands. The central nervous mechanisms which regulate the motility of the stomach may also be conditioned. For example, the pain caused by the insertion of a hypodermic needle will inhibit hunger contractions in the dog; but, after this is repeated a number of times, this pain no longer causes inhibition. However, if a new type of pain stimulus is applied, motility will be inhibited. In this instance, the dog has been conditioned to "ignore" the apprehension associated with the pain. He no longer fears that the pain may cause injury. After adequate training the dog can be subjected to a number of different types of mild pain stimuli, noises, etc., without inhibition of motility of the stomach. The dog no longer fears that he will be injured.

This raises the old question of whether the autonomic motor control of the digestive tract has representation in the cerebral cortex. Fulton and his associates[1] have recently reported that stimulation of the premotor area of the cortex in monkeys and chimpanzees results in vigorous movements of the intestine. They believe that this provides an explanation for the morbid hunger and intussusceptions which sometimes develop after bilateral extirpation of the premotor areas. The facts that on the one hand sleep and decerebration (King, in guinea pigs) augments motility and on the other hand dreams and apprehension usually inhibit motility[2], indicate that the primary influence of the cerebral cortex on motility is inhibitory in nature. The exaggerated motility on stimulation may indicate a release of lower autonomic centers from cortical inhibitory control, rather than direct stimulation. Nevertheless, the facts clearly indicate that cerebral activity may result either in an augmentation or an inhibition of gastro-intestinal activity.

What are the observed effects of anxiety and emotion on the motor activity of the stomach? The inhibitory effect of

anxiety and anger was first directly observed in man by Beaumont. It was later studied in some detail in lower animals by Cannon[3] and Carlson[2].

As a general rule apprehension inhibits both the motility and secretion of the stomach. In lower animals no one, so far as I know, has seen any other effect. In man, radiologists[4] know that apprehension or mental shock causes the stomach to "drop" and become "flatter" in contour. I personally have seen the stomach of students drop in response to a threat and rise again and resume motility on provoking laughter by passing the threat off as a joke. Gastric emptying is definitely delayed by quizzing a poor student. It is not usually delayed by quizzing a good student who has faith and confidence in his ability to answer questions correctly. However, I am quite certain that occasionally strong emotion may cause spasm and hypermotility of the stomach without nausea and vomiting being experienced. The literature, in so far as actual evidence is concerned, is silent. Alvarez[5] has told me of two patients suffering from pain in the epigastrium following strong emotional stress in whom he made x-ray studies. In both instances he observed five or six deep waves passing over the stomach simultaneously, the stomach presenting the appearance of a sock filled with billiard balls. I have seen a similar picture in a hysterical young woman, in which detailed examination and other considerations revealed that the disturbance was not due to a viscero-visceral reflex or organic disease. Thus, it would appear that apprehension as a general rule leads to an inhibition of motility, but may in some subjects result in marked hypermotility and tonus of the stomach.

Todd[6] has made the most intensive study to date of the effect of anxiety on the human stomach. His subjects were medical students. He started his studies during the early apprehensive weeks of the "new life" of a modern medical student and continued with the same students for several years. He has reported that the "stable stomach"

does not respond readily to emotional factors and is found in persons with an "even temperament." Many of his first year students manifested an "unstable stomach" in that "dropping" and inhibition of movements of the stomach occurred when subjecting them to emotional factors. The stomachs of his second year students were more stable. Thus, as shown in the "pain" experiments on the dog cited above, through training or conditioning, the stomach may no longer be affected by inhibitory psychic factors. A more significant observation, however, was made, namely, that when the conditioned or trained stomach shows instability in response to more prolonged mental distress, the instability takes the form of hypermotility. Todd has stated: "hyperactivity of the stomach is always present in the anxiety complex and in patients consciously or subconsciously nervous but not afraid."

Over what nerves are the above effects transmitted to the stomach? Before this question can be clearly answered it is necessary to consider briefly the functional innervation of the stomach. Much of the recent work on this subject is confusing to the average reader. This is because of the actual complexity of the functional innervation of the stomach. For example, both motor and inhibitory effects may be obtained via either the splanchnics or vagi[7]. However, one must not permit details, although important, to fog a true conception of the predominating functional innervation of these nerves.

By sectioning the splanchnic nerves in dogs, it has been shown that psychic inhibition of gastric motility is almost entirely abolished[2]. This leads us to believe that the splanchnic nerves are primarily concerned in the psychic inhibition of gastric motility and tone.

But, the mechanism concerned in the production of the augmented motility that Todd reports as occurring in the unstable, conditioned stomach in the presence of sustained anxiety is not so clear. This is because such a condition has never been produced in lower animals in which the nerves may be experimentally sectioned. The vagi very probably

are primarily concerned, because of the following considerations. They are the predominant motor nerves of the stomach. Following section of the vagi in animals a permanent hypotonus and delay in evacuation of pastes and solids results[8], though liquids may soon be evacuated in normal time. Following section of the splanchnic nerves in man colic may occur which is relieved by atropine[9].

In spite of Crile's[10] interesting theories it is difficult to believe that this hypermotility and tonus is induced chiefly by the splanchnic nerves. However, it is true that spasm of the pyloric sphincter may be induced reflexly via the splanchnic nerves and that epinephrine in adequate dosage causes the sphincter to contract[11]. It is possible that given a contracted sphincter, the stomach will manifest compensatory vagal hypermotility. But, epinephrine inhibits gastric motility. (No one has studied the effect of psychic factors on the pyloric sphincter.) It is also pertinent that stimulation of the splanchnic causes vasoconstriction of the gastric vessels. This means that in anxiety some constriction of the gastric vessels may occur and cause some asphyxial spasm of the gastric musculature; but this could not continue for any length of time in the fundus of the stomach in view of the continuance of the normal or hypernormal secretion of the hypermotile stomach. It is difficult to picture how the peristalses in the pyloric antrum could continue, since a mild degree of anoxemia inhibits motility, although it does induce spasm of the sphincter[12]. Of course, it may be argued, in so far as the etiology of "peptic" ulcer is concerned, that the hypermotility of sustained anxiety is due chiefly to the vagus and that this is associated with an increased splanchnic vasoconstrictor tone of the vessels of the mucosa. Because so much of the foregoing type of speculation is required in any attempt to rationalize the procedure of adrenal denervation for "peptic" ulcer, it is difficult for a physiologist to warm-up to the idea.

I have yet to meet a clinician of extensive experience who denies that sustained anxiety is a factor in determining the chronicity and recurrence of "peptic" ulcer in many cases.

In this connection, Todd[6] reports that students may have hyperactive tracts for several years without developing ulcer, but hyperactivity was evident in those of his students who later developed the symptoms of ulcer.

We[13] have recently attempted to determine in the dog whether the maintenance of continuous hypermotility and hypersecretion of the stomach for a period of two months will result in chronic ulcer. One group of animals was injected every two hours with pilocarpine, a second group with histamine, and a third group with both pilocarpine and histamine. Acute lesions of the stomach and duodenum were observed only with pilocarpine, but no chronic or perforating ulcers were produced.

It would appear from these studies in the dog that some other factor besides hypermotility and secretion is necessary for the production of a chronic "peptic" ulcer. It should be remarked that these animals were fed a "smooth" diet, and the results might have been different on a "rough" diet. These drugs, of course, would not have a "neurotrophic" effect or a vasoconstrictor action which are the only other factors which have been suggested as being concerned in the "anxiety-ulcer" relationship. That a "rough" diet and hypermotility and secretion are factors conducive to ulcer is generally recognized and has much experimental support.

The major facts pertaining to the functional innervation of the pyloric sphincter may be briefly summarized as follows: the sphincter usually contracts on noxious stimulation of the gall bladder, colon and appendix[11, 14, 15]. The motor side of this reflex is primarily in the splanchnics. At the same time the stomach is inhibited unless nausea and vomiting occur in which instance the antrum contracts via the vagi. The vagi are concerned in the inhibition of both the sphincter and stomach when the duodenum is mildly stimulated (enterogastric reflex)[16]. This mechanism normally retards gastric evacuation. In the instance of irritation of the duodenum, the local Meissner-Auerbach's plexus

is concerned in causing contraction of the sphincter without inhibition of gastric motility[16]. This mechanism may be concerned in the delayed evacuation with hypermotility in cases of duodenal ulcer. Cases of duodenal ulcer that empty more rapidly than normal are to be explained by the more rapid rate of emptying of the duodenum, associated with the hypermotility of the stomach.

Reflex pylorospasm and vomiting occur in dogs with splanchnics sectioned.

In regard to the autonomic innervation of the biliary tract, I shall only point out that atropine favors the flow of bile from the common duct and pilocarpine has the opposite action. Atropine decreases the tone of the gall bladder but does not prevent the action of cholecystokinin. Pilocarpine causes some contraction of the gall bladder, but no bile is expelled into the intestine because of the simultaneous increase in the choledochus duodenal resistance[17].

Passing on to the intestine there is a point pertaining to appetite and intestinal obstruction which demonstrates a significant function of the autonomic innervation of the gastro-intestinal tract. In a study of continuous jejunal alimentation in two dogs, we observed that as long as we kept the intestine filled with food the dogs showed no desire to eat in the normal manner. However, after sectioning the vagi these animals manifested an inordinate appetite even to the extent of coprophagia. This shows that the feeling of satiety depends to a large extent on the vagus and that distension or irritation of the intestine, like the stomach decreases appetite. This was shown more strikingly by Herrin and Meek[18]. They continuously distended an isolated loop of intestine. A very copious secretion of intestinal fluid resulted, the dog would not eat and drink, became dehydrated, developed hypochloruria and died. However, after the nerves of the loop were sectioned, the dog would eat and drink and survived in spite of the continuous loss of fluids and chlorides. This demonstrated that the prime factor in the serious consequences of simple obstruction without strangulation is the loss of water and chlorides.

A consideration of the motor innervation of the ileo-cecal sphincter is of practical importance in that it may explain ileo-cecal intussusception that sometimes occurs in infants and after appendectomy in adults. The sympathetic supply of the ileo-cecal sphincter is definitely motor in its function. The vagi have both a motor and inhibitory effect on the sphincter, which, however, is slight when compared to the motor effect of the sympathetic[19]. If, during or following appendectomy the sympathetic supply to the sphincter and lower ileum is sectioned or affected, the sphincter will become patulous and the lower ileum hypermotile. This would increase the likelihood of the ileum undergoing intussusception into the cecum. Ileo-cecal intussusception is the most common type in the infant. According to Zamorani[20] the coeliac ganglion does not mature histologically until about two years of age. If this is true physiologically, we have the explanation for the clinically observed vagotonic tendency of the infant's gastro-intestinal tract. In addition the infant would have an atonic ileo-cecal sphincter which with a hypermotile ileum would predispose to ileo-cecal intussusception.

Our knowledge of the functional innervation of the colon of man is rather sketchy. We know much more concerning this subject in lower animals. Because of the rather marked anatomic differences some physiologists have hesitated to apply their work to man. However, this reticence is not entirely justified as has been demonstrated by the recent surgical treatment of Hirschsprung's disease. For years physiologists have known that the predominant parasympathetic effect was excitatory for the colon musculature and inhibitory for the sphincters, and that the predominant sympathetic effect was inhibitory for the colon and excitatory for the sphincters. It now appears to be established that section of the sympathetic supply of the colon in Hirschsprung's disease markedly alleviates the obstipation. The obvious result is relaxation of the smooth muscle sphincters of the colon and an increase in the propulsive activity of the colon.

Physiologically I believe the irritable or "unstable" colon is quite analagous to the "unstable" stomach which was discussed above. Clinically it is recognized that many "peptic" ulcer patients have an "unstable" colon. In both conditions belladonna, bland diet and sedation are used therapeutically. In regard to the "unstable" colon and cecal stasis a physiologic fact that is not fully appreciated is that the colon throughout its course manifests the phenomenon of receptive relaxation. This is true for the rectum as is well known. It is particularly true for the cecum. It is also true of the transverse and descending colon. The application of this fact, I believe, is obvious.

In certain abnormal conditions of the colon large quantities of mucus are produced. The evidence indicates that this is not due to a direct stimulation of secretion by nerves. However, prolonged stimulation of the pelvic nerves, repeated injection of pilocarpine, or the introduction of irritants into the colon increases the production of mucus. This would indicate that the augmented secretion is chiefly due to irritation of the mucosa and excessive motility. Extracts of the colonic mucosa according to Florey[21] do not increase mucus production.

It is of clinical interest that fear or apprehension causes pallor of the mucosa and of the colon, even in the absence of the adrenals[22]. If an area is inflamed, pallor does not result. This pallor is due both to a general contraction of the vessels of the mucosa and to a squeezing out of blood by contraction of the muscularis mucosae. The colon, on mechanical stimulation, shows a patchy pallor due to irregular contraction of the muscularis mucosae.

I next desire to discuss briefly some of the more important viscero-visceral reflexes. I shall not mention the important viscero-skeletal or viscero-somatic reflexes.

It has been well demonstrated that the sympathetics conduct sensory sensations responsible for the elicitation of visceral pain, muscular rigidity, cutaneous hyperesthesia and vasomotor disturbances[23, 24]. The vagi conduct sensa-

tions which elicit nausea and vomiting, affect appetite, and which in the case of the stomach mediate impulses that are responsible for satiety. The sensory pathway for crude heat and cold sensations from the stomach is not known. These nerves also mediate sensory impulses concerned in viscero-visceral reflexes. The pelvic nerves are mixed in regard to their sensory activity.

Gastro-ileo-colic and Duodeno-ileo-colic reflexes: When food is ingested a reflex is initiated from the stomach and especially from the duodenum which causes rather rapid evacuation of the distal ileum into the colon. This, in all probability, increases the activity of the colon. This in turn accounts for the early post cibum distress of the patient afflicted with a colitis.

The importance of this reflex did not impress me until several years ago when we made a study of the ileo-cecal sphincter. We observed that when some barium milk was placed into the distal ileum of a fasting dog through an ileostomy, it was retained there for one-half hour or longer. After the ingestion of food, the barium milk was evacuated into the cecum within fifteen minutes. The nervous mechanism of this reflex has not been determined.

Cholecysto-gastric reflexes: Recently Fishback and I studied[25, 2, 15] the effect of biliary tract distension and irritation on the movements of the stomach. We observed that mild stimulations inhibited gastric motility and decreased tone. This type of response, according to my views, is conducive to gastric flatulence and air swallowing. A sudden marked distension caused pylorospasm with nausea and vomiting. This accounts for the dyspeptic symptoms of gall bladder disease. But, the pain of biliary colic is not due to pylorospasm because the type of referred pain is different and biliary tract pain may be obtained in man and dog following subtotal gastrectomy[17].

Appendico-gastric reflex: The fact that the diseased appendix may reflexly affect the stomach is indirectly one of the reasons why the mortality of appendicitis is still so high in this country. The lay person thinks the symptoms are

due to a "stomach upset" and takes a physic or enema, which results in rupture and peritonitis. The physician, if called early, can save the life of practically every patient with appendicitis.

Experimentally distension of the appendix and cecum in the dog results in inhibition of the gastric movements chiefly via the splanchnic nerves[2] (also Bussabarger & Ivy). The pyloric sphincter generally contracts—an effect that is mediated chiefly via the splanchnics also. (Inhibition of the sphincter may also result)[2, 15]. Marked distension of the appendix and cecum particularly if the latter is irritated causes pylorospasm and frequently vomiting. Under such conditions it is difficult to determine whether the dog suffers epigastric pain or not. Dr. Livingston of New York has written me that when the appendix in man is distended, epigastric pain, nausea and sometimes vomiting result. Right lower quadrant pain, point tenderness and cutaneous hyperalgesia followed immediately. In this connection Loreti[26] has reported that after anesthetization of the right lower quadrant the pain in that segment disappears, but the epigastric pain persists.

Of course, epigastric pain does not always occur in appendicitis. Neither can the same type of viscero-visceral reflex always be elicited with the same stimulus in dogs. This must mean that either the reflex threshold is very high or other factors inhibit the reflex.

Smith[15] has found in patients that distension of a spastic colon may produce gastric spasm with severe epigastric pain, which is not elicited after atropine. This again indicates, as referred to above, that spasm of the pyloric antrum in contradistinction to the pyloric sphincter is due chiefly to the influence of the vagus.

It should also be borne in mind that irritation of the colon, cecum and appendix reflexly causes the ileo-cecal sphincter to contract. This has been demonstrated in animals[19] and ileal stasis has been observed in man by Hunt, Cole and Kantor[27].

Reflexes between the genito-urinary and gastro-intestinal tracts: Reflex changes in the stomach analogous to those described above may be elicited by stimulation of the genito-urinary organs[2, 28]. This should be borne in mind because patients have been treated for "dyspeptic" symptoms when the real source of their trouble was resident in the urinary tract.

Time does not permit me to proceed further. Such rather interesting and important gastro-intestinal viscero-visceral reflexes or effects as the colon-duodenal, viscero-cardiac[29, 30, 31] and reflexes within the colon itself [32] may be mentioned in passing.

Often when I contemplate the many mechanisms in the gastro-intestinal tract that may get out of order, and the fact that mental activity may throw some of them out of order, I think of the statement of Josh Billings, to wit, "I have finally kum tu the konklusion that a good reliable sett of bowels is worth more to a man than enny quantity of brains."

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LIBRARY NOTES

EARLY LETTERS OF WILLIAM BEAUMONT NEVER BEFORE PUBLISHED

The one hundredth anniversary last year of the publication of William Beaumont's work on digestion brought into prominence the life of the military surgeon who had been neglected by posterity for many years. During the exhibit on that subject at the Academy in the fall, Dr. Irving Pardee was kind enough to present to the Library a letter written by Beaumont and a miniature of him as a young man, both of which had come down in the Beaumont family to Miss Lotta E. Hale of Hartford, Connecticut, great-great-niece of William Beaumont. We were also fortunate in the loan of four Beaumont letters by Mr. Hugh McLellan of Champlain, N. Y., who has given us his permission to publish them.

All four of these notes were addressed to Pliny Moore, Esq. of Champlain, distinguished judge of Clinton County for seventeen years. He was a descendant of a Deacon John Moor who left Dorchester, England, in 1635 and settled in this country. As a young man, Judge Moore enlisted in the American army, and in 1777 went to Canada with Benedict Arnold. He was later commissioned lieutenant by Gov. Clinton and served until the end of the war. At the close of the war he bought a large tract of land in Champlain and became an influential, highly respected figure. Beaumont's first three letters to him bear the dates November 2, 1807, 23 March, 1808 and 5 February, 1809. During the years 1807 to 1810 Beaumont taught school in Champlain and tended store. These two activities did not hinder him from other interests, as in 1807 he was serving as secretary "Pro tempore" of the Champlain Select Debating Society. He writes to Moore, "I have the pleasure to inform you that you are elected an honorary member of this society by the unanimous voice of the society and agreeable to our laws. Your attendance is solicited, and will be amicably accepted, on the evenings of Tuesday, in each & every week,

at six o'clock P. M., at Tyler & Beaumont's store. By order of the President's request of the Secretary and permission of the Society." The note of 23 March, 1808 is reproduced here. It is interesting to see his flourishing penmanship, possibly the result of his year as a schoolmaster.

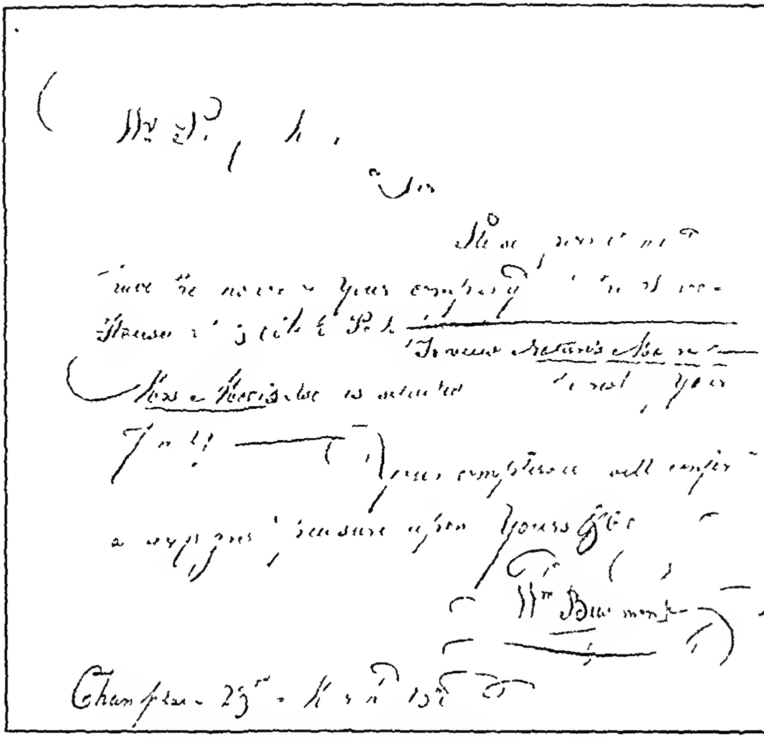
The letter written in 1809 indicates that Beaumont's early as well as his later years were troubled by controversy. "Honored sir: Not having an opportunity of tracing to the origin the crime which you partially alleg'd against me Saturday last, I am prompted by a sense of truth, honor, humanity, & justice to myself, to solicit a farther investigation of the subject, as I feel as tho' there were an injury done someone by such an attrocious, ungrateful & inhuman idea, as that of abusing & beating a child to such an unmerciful degree as has been asserted—and, sir, I wish to have the truth known & the aggressor punished. I stand ready & am willing & free to have my conduct in general, & my treatment toward the school in general or any individual of it, thoroughly inspected & critically investigated—& if I be the person guilty of such an act of atrocity as alluded to above, I justly deserve to be banished from the school, driven from society & punished with eternal neglect. I hold myself amenable to truth & am ready to stand its test—but a sense of inocence & a peaceful quiet conscience avert the fear of shame or aprehension of guilt.

"But if such be the assertions it behoveth me to know the author or the instigator & give a chance to him or his advocates to make true or fals the report & if it come from a child old enough to know or judge between right and wrong, it ought not to escape with impunity, & sir, if you be the parent of the child who deals thus largely in unfounded & inhuman falshood, you alone are the proper person to correct or reform him. If you do it not, I wish you to relieve me & deliver the school from the dangers & disturbencies which will arise from such circumstances. I make no words untill further inquiry into the origin of the affair. But there is an attrocious absurdity in existance either the act alleged, or the report asserted, one of which

must be substantiated before your own mind, your family's or mine can be at ease or rest satisfied.

"Your condescension of letting me hear from you on the subject soon, will command that attention & respect which is due from youth to age, honor & respectibility." Since the town records and school records were destroyed by fire, it is impossible to learn the outcome of the case, unless yet undiscovered correspondence comes to light. As he taught school there for still another year, we can assume he was exonerated. No doubt his rhetorical style came from his experience with the Select Debating Society.

It may be of interest to note that these three early letters give the spelling "Moor." Judge Moore was the first to add the final "e" to the family name, and the letter Beaumont addresses to him in 1820 has the new spelling. The subject of the note which is here reproduced, Samuel Long, came from Danville, Vermont. He was a carder of wool in the employ of the Judge. In January, 1819, while passing through Lyndon, Vermont, his carriage was upset and his thigh broken in two places. The physicians who attended him succeeded only in torturing the patient and did not even discover the second break. In May Long returned to Champlain with one leg three inches shorter than the other. The next step was to bring suit against the two doctors who were responsible for the condition, Dr. Calvin Jewet of St. Johnsbury, Vermont, and a Dr. Fields of London. A letter from Long, dated Jan. 26, 1820, reads, "By the advise of Mr. Vanness, Wee have agreed to submit it to a rool of Cort. Wee have agreed on three men, doct. Beaumont of Plattsburgh & doct. Wood of Champlain are the two that I have chose & doct. Powel of this place [Burlington] is their man . . ." The case was not brought to trial until June, 1820, and by that time Beaumont was in Michigan. On March 18, 1820, he was commissioned Post Surgeon by President Monroe and ordered immediately to Mackinac. He left Plattsburgh on May 6 of that year and so was not on hand to testify at the trial.



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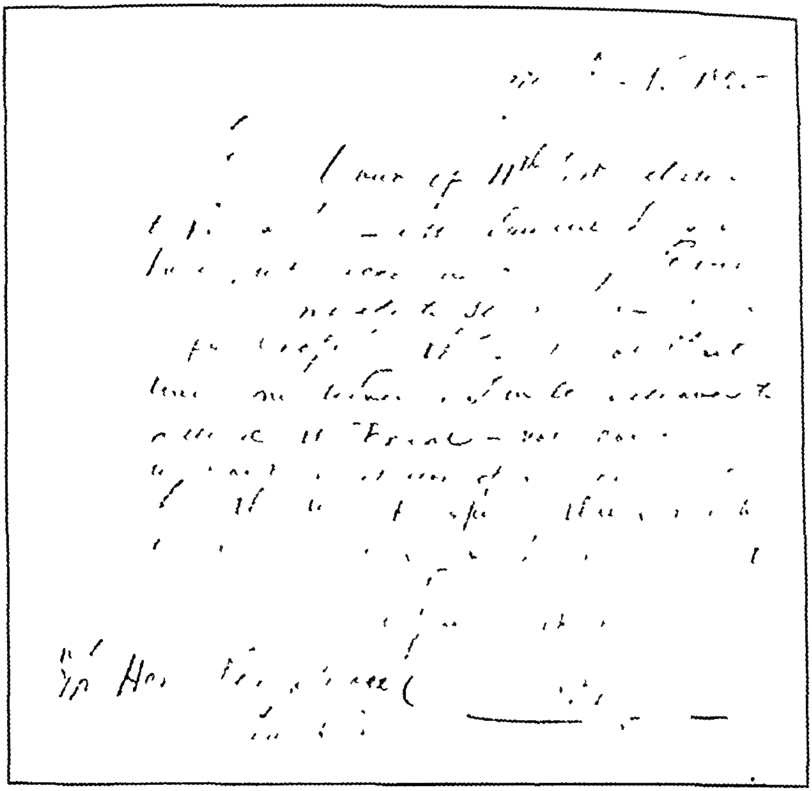
Mr. Hugh McLellan of Champlain

On May 30 of the same year, Beaumont wrote to his brother Abel from Niagara Falls, as he was en route to Mackinac. This letter is the gift of Dr. Pardee. "Having a minute or two liesure & knowing your wish to hear from me, I avail myself of the opportunity to say that I am well, & progress regularly on my rout—from Hartford, I proceeded to Albany & then directly on to Utica, when I took passage on the Great Western Canal in one of the boats, her first trip. I passed 82 miles to Montezuma in her. It is a most delightful way of travelling & goes at the rate of 5 miles an hour on perfectly smooth water—drawn by two elegant horses & you have all the accommodation of a steam boat without that confusion, or the least danger of accident. From there I proceeded to Buffalo in the stage—fell in company with the Rev. Doct. Morse—author of the Uni-



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versal Geography & his son going on to Mackinac on a mission among the Indian tribes by order of the Government. He is a fine old gentleman & I probably shall have his company all the way, he being desirous that I should accompany him as far as I go on account of his health. Yesterday we came here to view the falls—that wonderful curiosity that he has very accurately described in his geography, though he had never seen them till now. He seem as much astonished at the view as though he had never heard of them, they so much surpass his expectations. You probably will see, e'er long, another great description of them. I believe he is making a new edition of his former geography from what I can collect from conversation. We go from here after we have crossed over the bridge to Goat Island & back & return to Buffalo & take the SteamBoat for Detroit, tomorrow morning.

"This must suffice for the rest of the family at present. Have the goodness to transmit it to them when you have perused it. Encourage John in his agricultural pursuits as much as you can. He will do well if he don't get discouraged. Look out for sharpers & take care of yourself. My respects to Mr. Francis & others, believe me, Your affectionate brother." A postscript reads, "Let me hear from you at Mackinac. I shall be there in a few days."

The "Dr. Morse" he mentions is Jedidiah Morse, born in Woodstock, Conn. in 1761 and died in New Haven in 1826. Although a clergyman, he is known now as the "Father of American Geography." He may also be remembered as the father of Samuel F. B. Morse, founder of the American system of electromagnetic telegraph. Another son, Richard Cory, 1795-1808, who made a name for himself as a journalist, was at one time a student of theology, and was probably the son referred to by Beaumont.

Further details of his trip are recorded in his diary, a large part of it having been published in Myer's *Life and Letters*. It is in such material that we get intimate glimpses into the lives and characters of great men whose memory should be honored and fostered.

GERTRUDE L. ANNAN.

RECENT ACCESSIONS TO THE LIBRARY AND MUSEUM OF THE NEW YORK ACADEMY OF MEDICINE

The Books and Instruments of John Greenwood

Often I am asked the question, "What is there so interesting that induces you to continue year after year as Librarian?" My answer usually is "The uncertainty, thrills and surprises that one receives."

In the series of books issued in the American Journal and Library of Dental Science, 1845, there appeared the translation of another of Delabarre's work on "Second Dentition," 1819, by Chapin A. Harris.

Greenwood, in the same year, wrote a work of 227 pages, which was entitled "Treatise Upon Dentition and the Manner of Cleansing, Scraping, Filing, Plugging and Extracting the Human Teeth" and illustrated by the author. This unpublished manuscript, we hope, will now be printed. Besides the above-mentioned accession, there is the professional card, containing the likeness of John Greenwood, made by Roy in Paris in 1806.

Priceless as are the books, more so are the instruments and engine. The dental instruments were made by John Greenwood and used by him and his son. The top row are the operative, while the lower are those used in constructing the ivory artificial dentures. Several of the ivory handles of the operative instruments have carved upon them "Do not touch." Even John Greenwood considered them of great value, and so they have been preserved all these years.

The foot engine, perhaps the first so constructed, as at that time only the bow drill was used, was made from a spinning wheel and antedates Wilkerson's and Black's by some eighty years. Accompanying the wheel is the following note:

This is the spinning-wheel of Elizabeth Weaver, wife of Doctor John Greenwood, dentist of New York.

It belonged to her grandmother, Elizabeth Hoogland who married Joris Cosaart of New York and Somerset Co., N. J. Their daughter, Jane Cosaart married William Weaver of New York, whose daughter Elizabeth married John Greenwood, 22 March 1788. The spinning-wheel must be almost two hundred years old.

In the *Dental Cosmos* of October 1906 an article by Edward C. Kirk, D.D.S., *Original Communications,* gives the following: "A letter from his (John Greenwood's) son, Dr. Isaac J. Greenwood to Jonathan Taft in November 1860 gives many interesting details of the methods of practice pursued by his father. . . In the same letter he states—'my father was the first to use the foot drill, and he made it himself from an old spinning-wheel of my grandmother's, and since his death I myself used it—the same one—altogether in my practice for twenty years, and have it yet.' This device would seem to have been the direct American ancestor of the dental engine."

Dr. Isaac J. Greenwood whose letter is here quoted died May 14, 1865. The spinning-wheel came to me from his eldest son, my father, Isaac J. Greenwood, 2d, who died 16 December 1911.

(Signed) Eliza R. Greenwood.

BERNARD WOLF WEINBERGER.

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NOVEMBER 9

The recognition and treatment of peripheral circulatory failure (Shock).

Clinical differentiation between cardiac failure and peripheral circulatory failure—rôles of decreased circulating blood volume and increased capacity of the vascular bed—clinical pictures characterized by diminished venous return to the heart—the occurrence of peripheral circulatory failure: traumatic and postoperative shock, infections and intoxications, anaphylactic states, dehydration and hypochloremia, coronary thrombosis, diabetic coma, etc.—treatment of peripheral circulatory failure.

ARTHUR M. FISHBERG, *Associate in Medicine, The Mount Sinai Hospital.*

NOVEMBER 16

The therapeutic and toxic actions of some drugs recently introduced in the treatment of cardiac disorders.

A critical examination of the claims made for a number of drugs used in the treatment of heart disease will be made. The range of therapeutic dosage and the undesirable toxic actions will be discussed. Particular attention will be given to those drugs that affect the cardiac rate and rhythm, and to the so-called coronary vasodilators. ARTHUR C. DeGRAFF, *Samuel A. Brown Professor of Therapeutics, University and Bellevue Hospital Medical College.*

NOVEMBER 23

Signs and symptoms in abdominal diagnosis. (Lantern Slides)

A. Analysis of the Clinical Syndrome.

(1) The basic nature of manifestations of abdominal disease; essential unity of clinical and laboratory data. (2) Different relative value of signs and symptoms in various intra-abdominal affections; examples, peptic ulcer vs. gastric cancer, acute appendicitis vs. ruptured corpus luteum cyst, mechanical intestinal obstruction vs. mesenteric thrombosis. (3) Classification of signs and symptoms; mechanical, humoral and neurogenic phenomena in practical diagnosis; illustrations, abdominal tumors, biliary tract diseases, cirrhosis of liver, intravisceral lesions vs. peritonitis. (4) Abdominal rigidity and cutaneous hyperalgesia; abdominal manifestations of extra-abdominal lesions. (5) The experimental approach to clinical problems; motion picture demonstration of ureteral and gastrointestinal visceral reflexes.

B. The Differentiation of Clinical Syndromes.

(1) Methods in differential diagnosis; merits of each; their relationship. (2) Multi-method approach to individual case study; a chart. (3) The fundamental law of differential diagnosis; specific applications.

EDWARD M. LIVINGSTON, *Associate Visiting Surgeon, Bellevue Hospital.*

DECEMBER 7

The interpretation of low back pain and its treatment. (Lantern slides)

I. A discussion of the predisposing factors in low back pain. a. Body form and muscular development. b. Anatomical variations. c. Occupational or sudden trauma. d. Unrecognized arthritis or other diseases.

II. Methods of examination helpful in establishing a correct diagnosis as to the precipitating cause and the exact location of the lesion which gives rise to the symptoms.

III. A discussion of treatment appropriate to the elimination of background and foreground causes and the relief of immediate discomfort by operative and non-operative methods.

ROBERT B. OSGOOD, *Emeritus Professor of Orthopaedic Surgery, Harvard Medical School.*

DECEMBER 14

The handicapped child.

A discussion of the more common ailments of childhood in their relation to physical and mental development. Attention will be called to physical and mental defects of ductless gland origin, to infections of the upper respiratory tract, gastrointestinal disorders and anomalies, postural errors, environmental conditions.

CHARLES G. KERLEY, *Consulting Pediatrician, Babies' Hospital.*

DECEMBER 21

The significance of excision in the treatment of local tuberculosis in bones, joints and lymph glands as exemplified in the treatment of tuberculosis of the thoracic wall.

The significance of local tuberculosis in bone, joints and lymph glands; phases of tubercular infection; relation of these lesions to lung tuberculosis; relation of bovine tuberculosis; aims of surgical treatment; relation of excision to arrest of local lesions and to local healing; relation of immobilization to local healing; danger of dissemination by excision; illustrative cases in tuberculosis of costal cartilages, ribs, mediastinal glands and clavicles.

WALTON MARTIN, *Professor of Clinical Surgery, College of Physicians and Surgeons.*

DECEMBER 28

Present status of the prostatic problem.

Recent investigation relative to the etiology of prostatic hypertrophy. Earliest symptoms of prostatic obstruction, importance of diagnosis of prostatic pathology. Modern methods of treatment.

HENRY G. BUGBEE, *Attending Urologist, St. Luke's Hospital.*

1935

January 4

The recognition of the early symptoms of brain tumors.

The significant clinical symptoms which may be indicative of a brain tumor in the early stages of its development; also cases in which there have been very few, if any, premonitory symptoms; cases where there has been unnecessary attention paid to sinus disease or to the gastro-intestinal tract where after there had been a careful examination and a proper consideration of all the clinical symptoms a brain tumor would have been diagnosed early instead of late in its course.

ISRAEL STRAUSS, *Attending Neurologist, The Mount Sinai Hospital.*

January 11

The diagnosis and treatment of meningitis.

A brief consideration of symptomatology and differential diagnosis of the various forms of purulent meningitis. Importance of the examination of the spinal fluid.

Discussion of types of meningococcic meningitis with reference to indications for treatment. When should serum be used intravenously? The routine use of serum intraspinally. Problems involved when the patient fails to respond to the routine treatment, with special reference to over-treatment and to the development of block.

Difficulties involved in the treatment of other forms of purulent meningitis. Comments on the best methods of treatment available at the present time.

JOSEPHINE B. NEAL, *In charge of the Division of Applied Therapy, Bureau of Laboratories, Health Department, New York City.*

January 18

Bulkley Lecture: *The relationship of trauma to malignancy.*

The rapid increase in the knowledge of the effective exciting causes of different malignant tumors calls for more rigid criteria by the medical profession, regarding the relation of trauma to cancer. One may no longer rely on the vague statement that we do not know the causes of cancer, and therefore, we may assume the importance of trauma whenever asserted. One must still proceed on the assumption that trauma may be capable of exciting a large variety of malignant tumors, but one must demand more rigidly than ever before, that the evidence favoring trauma is fully established, and that other better known causes are not present. This policy excludes any general statements regarding trauma and cancer, and demands that the evidence should be rigidly considered with each particular type. The lecture endeavors to present the present available data regarding the relation of trauma to some of the more important types of cancer.

JAMES EWING, *Director of the Memorial Hospital.*

JANUARY 25

Points in medical diagnosis.

Methods of diagnosis and differential diagnosis that a long experience has proven to be of value. Stress will be laid upon conditions in which laboratory methods are not of decisive aid. The affections touched upon will be mainly those of the chest and abdomen, in particular those of the diaphragm, gallbladder, pancreas, appendix, and kidney. EMANUEL LIBMAN, *Consulting Physician, The Mount Sinai Hospital.*

FEBRUARY 1

Carditis in children.

Frequency of rheumatic carditis. Occurrence without other manifestations of rheumatic fever. Symptoms and signs of subacute and subclinical phases. Differential diagnosis. Public health aspects. Necessity for recognition of subclinical forms, and early diagnosis. Prognosis. Treatment. Methods for control.

LUCY PORTER SUTTON, *Assistant Professor of Pediatrics, University and Bellevue Hospital Medical College.*

FEBRUARY 8

Recent advances in cardiology.

A critical review of some of the more important contributions to cardiovascular physiology and disease in recent years. Recent contributions to medical and surgical therapy of vascular disease, anginal and congestive heart failure. Brief comment upon increasing knowledge of, and limitations of the electrocardiographic method.

H. M. MARVIN, *Associate Clinical Professor of Medicine, Yale University School of Medicine.*

FEBRUARY 15

Tumors of the breast.

All tumors of the breast are not cancerous but should be considered as such by the physician and the patient until definitely proven otherwise. The proportion of benign to malignant tumors in a large series of cases was given five to four. Treatment in any stage except early, is still unsatisfactory. In view of our present knowledge the only hope of lowering this high mortality is based upon a scientific suspicion of all breast tumors, their early and complete removal, radiation and a very careful "follow-up" of the individual.

ARTHUR M. WRIGHT, *Professor of Surgery, University and Bellevue Hospital Medical College.*

MARCH 1

Clinical aspects of nephritis and hypertension.

A pathogenetic classification. Clinical recognition of each type. A composite scheme for testing kidney function. Uremia. Prognosis. Treatment of cardiac and renal edema. An evaluation of drug therapy in essential hypertension.

WILLIAM GOLDRING, *Assistant Professor of Clinical Medicine, University and Bellevue Hospital Medical College.*

MARCH 8

The management of late syphilis. (Lantern Slides)

A lantern slide demonstration of late cutaneous syphilis, and syphilis of the bones, viscera, etc. A discussion of the importance, diagnosis and prognosis of late syphilis; latent syphilis; late congenital syphilis; general manifestations of cardiovascular, cerebrospinal and visceral syphilis. A description of relatively benign, dangerous and destructive lesions with symptomatology. Marriage and childbirth. Serology. Treatment—routine therapy outlined and modified according to age, duration, serology, past treatment, character of lesion, parts involved, latent or active, and other indications. Therapeutic indications and contraindications. Danger signs.

GEORGE MILLER MACKEE, *Professor of Dermatology and Syphilology, New York Post-Graduate Medical School.*

MARCH 15

Bronchoscopy, its value in the practice of medicine.

The value of bronchoscopy in conditions of the chest is given from the standpoint of its daily practical application. Its value in the clarification of obscure clinical symptoms, physical signs, or x-ray findings is stressed and examples of such experiences are demonstrated and cited.

MERVIN C. MYERSON, *Director of Otolaryngology, Kings County Hospital.*

MARCH 22

Leukemia—diagnosis and treatment.

Classification of various forms of leukemia from the aspect of clinical manifestations and hematological findings. Diagnosis. Treatment: The use of deep x-ray radiation, radium pack and arsenic in large doses will be considered in some detail.

JOSEPH E. CONNERY, *Associate Professor of Clinical Pathology, University and Bellevue Hospital Medical College.*

MARCH 29

Management and treatment of disorders of menstruation and the menopause.

A brief resumé of our present knowledge of the menstrual function. The various factors which may be involved in dysfunction. How these may be determined. Possibilities and limitations of treatment with special reference to the various endocrine preparations.

BENJAMIN P. WATSON, *Professor of Obstetrics and Gynecology, College of Physicians and Surgeons.*

APRIL 5

Sudden deaths with reference to their prevention. (Lantern Slides)

This paper deals mainly with autopsy findings in over 1,000 cases of sudden death from natural causes, and gives a summary of the lesions most commonly encountered in sudden, unexpected death.

Attention will be called to the very large number of deaths, chiefly in males, between the ages of 40 and 55. As 7 out of 10 of these deaths are due to organic heart disease, in which coronary arteriosclerosis and its sequellae play the most important rôle, the question arises: Are any of these deaths preventable? Their relation to over-eating, persistent driving of a tired body, over-play, hurry, anxiety, intense emotions such as anger, fright and worry, will be discussed.

Objection will be made to the popular belief that science can prolong the span of human life. It does, however, enable more people to live longer in the normal span. Men over 45 should endeavor to live their age and grow old gracefully.

HARRISON S. MARTLAND, *Chief Medical Examiner of Essex County, New Jersey.*

PROCEEDINGS OF ACADEMY MEETINGS

OCTOBER

STATED MEETINGS

The first Stated Meeting of the Academy for October, was omitted.

THE HARVEY SOCIETY (IN AFFILIATION WITH THE NEW YORK ACADEMY OF MEDICINE)
October 18

THE FIRST HARVEY LECTURE, "The Etiology of Pernicious and Related Macrocytic Anemias," Wm. Bosworth Castle, Associate Professor of Medicine, Harvard University Medical School.

This lecture takes the place of the second Stated Meeting of the Academy for October.

SECTION MEETINGS

SECTION OF DERMATOLOGY AND SYPHILOLOGY—October 2

I. PRESENTATION OF MISCELLANEOUS CASES FROM VARIOUS CLINICS.

II. DISCUSSION OF SELECTED CASES.

III. EXECUTIVE SESSION—Examination of cases is limited to members and their invited guests.

SECTION OF SURGERY—October 5

I. READING OF THE MINUTES.

II. PRESENTATION OF CASES—a. Demonstration of a fracture-orthopedic operating frame, Herbert Bergamini; b. Four cases of advanced carcinoma treated by electro-surgical methods, Tibor de Cholnoky; c. Six cases of inoperable malignant tumor six years after treatment with electro-surgery, George A. Wyeth; d. Three cases illustrating first paper of the evening, Frank L. Meleney; e. A case of gelatinous carcinoma of breast, C. W. Cutler, Jr.

III. PAPERS OF THE EVENING—a. The use of zinc peroxide in anaerobic and microaerophilic infections, Frank L. Meleney; b. Gelatinous carcinoma of the breast, George T. Pack.

IV. GENERAL DISCUSSION—Allen O. Whipple, Frank E. Adair.

SECTION OF NEUROLOGY AND PSYCHIATRY—October 9

I. PAPERS OF THE EVENING—*Acute Anterior Poliomyelitis*—a. Pathogenesis, Maurice Brody (by invitation), Arthur R. Elvidge, McGill University (by invitation); b. Immunization, William H. Park; c. Abortive cases as protective agents against epidemics, John R. Paul, Yale University School of Medicine (by invitation), James D. Trask, Yale University School of Medicine (by invitation); d. An experimental approach to the problem of resistance, C. W. Jungeblut.

II. DISCUSSION—John L. Rice, Josephine Neal, Frederick Tilney, Bernard Sachs, George Draper.

SECTION OF OPHTHALMOLOGY—October 15

I. INSTRUCTION HOUR, 7 to 8 o'clock—Diagnosis of muscle anomalies, James White, John Dunnington.

II. DEMONSTRATION HOUR, 7:30 to 8:30 o'clock—a. Slit lamp studies, Milton Berliner, Isadore Goldstein, W. L. Hughes, Girolamo Bonaccolto; b. Case examinations.

III. Section Meeting, 8:30 to 10:30 o'clock—a. Reading of the minutes; b. Case reports: 1. A case of unilateral exophthalmos produced by a meningioma in the middle cranial fossa, Martin Cohen, John E. Scarff (by invitation); 2. a. Case of fasciola hepatica with ovae in the vitreous; b. Metastasis in the choroid from carcinoma of the testis, Isadore Goldstein, David Wexler; c. Moving pictures, Charles N. Spratt, Minneapolis (by invitation); 1st reel: Enucleation with fat implantation, Removal of steel from anterior chamber, Removal of soft cataract by suction, Insertion of tube for lacrimal stenosis; 2nd reel: Glaucoma, sclerecto-irido-dialysis; 3rd reel: Cataract extraction—pocket flap method; 4th reel: Pocket flap cataract.

section of medicine—October 16

I. Reading of the Minutes.

II. Papers of the Evening—a. Artificial pneumothorax in the treatment of lobar pneumonia, W. E. Robertson, Philadelphia (by invitation); b. Pneumonias due to Pneumococcus Type XIV (Cooper): Occurrence, characteristics and serum treatment, Jesse G. M. Bullowa.

III. Discussion—Edgar Mayer (by invitation), William H. Park.

section of genito-urinary surgery—October 17

I. Reading of the Minutes.

II. Papers of the Evening—a. Tolerance, maintenance and protective dosage in urinary infection. Lantern Slides, Victor C. Pedersen, Discussion opened by Oswald S. Lowsley, Anthony Bassler; b. Urinary calculi. A clinical and experimental study, Lindwood D. Keyser, Roanoke, Virginia (by invitation), Discussion opened by Nathaniel P. Rathbun, Alexander R. Stevens, George F. Cahill.

section of otolaryngology—October 17

I. Reading of the Minutes.

II. Demonstration of the work of the New York League for the Hard of Hearing (in patient's room beginning at seven o'clock).

III. Papers of the Evening (8:30 o'clock)—a. The medical aspects of hearing conservation in New York City schools, Edmund P. Fowler, G. B. McAuliffe, Discussion by E. B. Faulkner; b. The physiological effects of physical therapeutics in otolaryngology, Richard Kovacs; c. A critical analysis of the methods of physical therapy in rhinolaryngology, Lee M. Hurd; d. A critical analysis of the methods of physical therapy in otology, A. L. Hollender, Chicago (by invitation), Discussion of the papers of Drs. Kovacs, Hurd and Hollender opened by Henry Hall Forbes and Harmon Smith.

section of orthopedic surgery—October 19

I. Reading of the Minutes.

II. Introduction to the treatment of scoliosis at the New York Orthopedic Dispensary and Hospital, Benjamin P. Farrell.

III. Presentation of patients illustrative of the treatment of scoliosis, Henry F. Ullrich (by invitation).

IV. Papers of the Evening—1. Preliminary treatment of scoliosis, Henry F. Ullrich; 2. Interpretation of roentgenograms, a. Measurement of angles, b. Determination of the primary curve, Albert B. Ferguson (by invitation); 3. Correction of the curve by plaster jacket, Henry F. Ullrich; 4. Determination of the correct area for fusion operation, Albert B. Ferguson; 5. The fusion operation, after-care and results, Henry F. Ullrich.

V. General Discussion—Samuel Kleinberg, Philip D. Wilson (by invitation), Joseph E. Milgram (by invitation).

SECTION OF PEDIATRICS

The October meeting of the Section of Pediatrics will be held on October 19th and 20th at the Hotel Ambassador in connection with the American Academy of Pediatrics (Region 1) and the Tri-city Pediatric Society. Morning session 9:30 a.m. and afternoon session 2 p.m. As the meeting will be clinical no program will be published.

SECTION OF OBSTETRICS AND GYNECOLOGY—October 23

The Section has decided to forego its October meeting in favor of the Graduate Fortnight. The program of the Graduate Fortnight for Tuesday evening, October 23, has been arranged by courtesy of the Section.

AFFILIATED SOCIETIES

THE NEW YORK ROENTGEN SOCIETY (IN AFFILIATION WITH THE NEW YORK ACADEMY OF MEDICINE)—October 15

I. 8:00 to 8:30 p.m.—Demonstration and discussion of interesting cases.

II. 8:30 p.m.—Errors in cholecystography and their correction—Wm. H. Stewart, H. E. Illick.

III. DISCUSSION TO BE OPENED BY—Ross Golden, Charles Eastmond, S. Fineman, William Snow.

NEW YORK MEETING OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE AT THE NEW YORK ACADEMY OF MEDICINE—October 17

I. Further experiments on effect of testicle extract on the agent of Chicken Tumor I—F. Duran-Reynals, A. Claude (Introduced by J. B. Murphy).

II. Protective substances in sera of animals injected with anterior pituitary-like hormone of teratoma testis urine—G. H. Twombly, R. S. Ferguson (Introduced by J. Ewing).

III. Successive transmission of virus of lymphogranuloma inguinale through white mice—A. W. Grace (Introduced by P. Reznikoff).

IV. Effect of Antuitrin S on circulating blood—S. H. Geist, F. Spielman.

V. Renal excretion of inulin, creatinine and xylose in normal dogs—A. N. Richards, B. B. Westfall, P. A. Bott.

VI. Inactivation and regeneration of glycolytic enzyme of muscle extract—L. Michaelis, J. Runnstrom.

VII. Epinephrine and blood sugar level—M. C. Hrubetz (Introduced by H. B. Williams).

VIII. Treatment of adult scurvy with crystalline Vitamin C. (ascorbic acid)—I. S. Wright (Introduced by W. J. Stainsby).

IX. Ovarian irradiation and sexual precocity in rat—J. Mandel, E. N. Grisewood (Introduced by H. O. Haterius).

I have also this further suggestion to make, and that is, that those of you who have any spare hours at any time of the day, especially during the mornings, make liberal use of the library of this Academy. You will be welcome and you will find it an excellent place for study and reflection.

I presume it is well for me to state that besides being the President of the Academy, I have been, these many years, an active Neurologist. I have a special interest, therefore, in one of the subjects, and if he does nothing else, I hope that the one speaker who is to discuss Functional and Nervous Diseases of the Stomach, will throw a little light on the supposed and much discussed nervous origin of peptic ulcer. I do not wish to prejudice the case, but I have found it rather difficult to accept some of the extreme views that have been promulgated on this subject, especially from the Middle West. However, I will bow to superior knowledge wherever it may come from.

Please regard these opening remarks as a mere appetizer. The substantial meal will be spread before you by others specially authorized to speak.

DEATH OF HONORARY FELLOW AND FELLOW OF THE ACADEMY

Ramon y Cajal, Santiago, Madrid, Spain; elected an Honorary Fellow of the Academy February 4, 1904; died October 17, 1934. Santiago Ramon y Cajal won recognition as one of the world's greatest neurologists. He was founder of the Histological Institute in Madrid. In 1906 he received the Nobel Prize in Medicine and Physiology, the only Spaniard to receive this award in any field of science.

Lusk, William Chittenden, B.A., M.D., 47 East 34 Street, New York City; graduated in medicine from Bellevue Hospital Medical College, New York City, in 1893; elected a Fellow of the Academy January 6, 1898; died October 24, 1934. Dr. Lusk was a Fellow of the American College of Surgeons and the American Medical Association, and a member of the County and State Medical Societies, the New York Surgical Society, and the Society of Alumni of Bellevue Hospital. He was Consulting Surgeon to Bellevue and St. Vincent's Hospitals and was for some time Professor of Clinical Surgery in the University and Bellevue Hospital Medical College.

BULLETIN OF
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EDITORIAL

LIFE AS AN OCCUPATIONAL DISEASE[1]

There is a well remembered witticism of Osler to the effect that "Everybody has a sane spot somewhere." Not a few observant men of letters, in fact, have been fain to envisage human life as commitment to or imprisonment in a lunatic asylum. The theme is implicit in every canto of the Inferno of Dante; it is sounded by Sancho Panza in Don Quixote and by Hans Sachs in the Meistersinger; it has been developed in simple scientific form by the French physiologist, Charles Richet, whose book ("Idiot Man") doubtless owes its title to Shakespeare's

> "Tale
> Told by an idiot; full of sound and fury,
> Signifying nothing."

"A Mad World, My Masters," the title of a play by one of Shakespeare's contemporaries, expresses the view entertained by most intelligent people with regard to the "cockeyed" or crackpot order of existence which had obtained since the World War. Leopardi saw the world as a freemasonry of knaves against honest people. Schopenhauer likened human existence to a penal colony, in which we are penalized for and expiate the blunders and stupidities of other people; a view of things which has fired many a bard of the Celtic or even the American world—

1. Read at the Medical School, Vanderbilt University, Nashville, Tennessee, on October 18, 1934.

"And the land is filled with bloodshed for the evils of the past,
And men will talk of justice as the storm of carnage raves,
And the innocent are punished for the guilty in their graves"

"Each prodigal life that is wasted,
In manly achievement unseen,
But lengthens the days of the coward,
And strengthens the crafty and mean.
The blood of the noblest is lavished
That the selfish a profit may find,"—

and how appalling that Bayard Taylor should have spoiled the rest of this momentous copy of verses by an abrupt lapse into Victorian bathos, unthinkable, unutterable, unprintable and unquotable!

Whether we incline to the gloomier or brighter side of things, it is obvious that at the back of the Darwinian struggle for existence lies the simple fact that each living creature is engaged in existing and asserting itself according to certain physiological laws which govern its being; nay, if we may credit some biological theorists, from Galen down, the very structure of its body is an expression of this remorseless will to live, this automatic and fatalistic functional activity. You will recall the old rhyme about the fleas which have greater fleas to bite 'em—"and so on *ad infinitum*"; or the quaint summation of professional jealousy in Bombastes Furioso:

"Myself have heard on Afric's burning shore;
A mightier lion give a mightier roar:
And the first lion thought the last a bore."

To physicians engaged in the practice of medicine, this particular slant on life has considerable value in connection with the reactions of individual patients to disease, injury or disaster. In the days of large families, the doctors of the past found the most astonishing differences in individual members of the group; and large families in the good old days often comprised a black sheep or n'eer do well, a fat boy or girl, a spoiled child, a village scamp or hero, a shiftless, sponging parasite, a lazy bones, a family slave, a competent flower of the flock and suchlike good, bad or

indifferent elements. The reactions of these different types of character to disease were, in the parable of a great naturalist, not unlike the effects of kicking a bull-dog, a mastiff, a Gordon setter, a spaniel, a terrier, a chow, a hound and so on. The same disease, as Billings observed, would "produce in one family convulsions, in another collapse, and, in a third, little or no danger or inconvenience."

Obviously the best frame for observations of this kind is that afforded by the study of disease with reference to occupations. The beginnings of this subject go back to remote antiquity. Even in the social order of ancient Egypt, it was noticeable that soldiers and gang laborers are exposed to wounds, communicable diseases and the effects of exposure; the upper ten to the effects of riotous living; the learned to the digestive, neurotic and ocular complaints of the sedentary. Hippocrates notes the diseases of fullers and wet-nurses and the ulcers of fishermen; Pliny the diseases of slaves. The hygienic rules or *Regimina* for travellers by sea and land, first outlined by Paul of Ægina and remarkably popular in the Middle Ages, were virtually tracts on occupational hygiene. Adjustment to life on board ship, particularly with reference to sea-sickness, is sometimes very much of an occupation. As early as 1473, there appeared an incunable by Ulrich Ellenbog on the effects of poisonous gases and fumes. Lobera de Avila published the first book on the diseases of courtiers, viz., catarrh, stone, gout and syphilis (1544), Agricola and Paracelsus wrote on diseases of miners (1546-67). But the assembly of the accumulated mass of scattered observations of this kind, within a definite framework, did not come to pass until the beginning of the 18th century.

About a year ago, there was celebrated, in the Italian cities, the tercentenary of the birth of one, Bernardino Ramazzini (1633-1714), the founder and father of industrial medicine and hygiene. Born three centuries ago, at Carpi near Modena, Ramazzini got his philosophical and medical training at Parma, and after some post-graduate work under Rossi at Rome, settled down to practice in

Modena (1671), where, in spite of some cold intransigence, he became eventually professor of theoretical medicine in the University (1682-1700). At the beginning of the new century, he was called by the Venetian Republic to succeed Sanctorius in the chair of medical practice at Padua, which, to the dismay of his fellow townsmen, he accepted at the age of 67. Fourteen years of successful teaching at this great medical center were hampered by attacks of cardiac palpitation, followed by a total blindness and a terminal apoplexy, which ended his days. Ramazzini died on his own birthday, November 5, 1714, exactly 81 years old, and a victim of the peculiar diseases of the learned which he had described so well. Like all the outstanding physicians of his time, he was a versatile polyhistorian. Poet, philosopher, erudite, clinician, epidemiologist, medical meteorologist and sanitarian, he wrote on epidemic lathyrism (1691), the water supply of Modena (1692), personal hygiene (1710), the Paduan cattle-plague (1712), the abuse of cinchona (1714); but his fame rests securely upon the little book on trade diseases, which appeared just after his accession to the Paduan chair (1700). A product of the Iatro-Chemical School and the work of a profound scholar, this book passed through seven subsequent Latin editions, and was translated into Italian, French, English, German and Dutch[2]. To give some notion of its scope and originality, it is only necessary to list its contents. In the first edition, Ramazzini devotes separate chapters to the diseases of:

1. Miners and gilders (*metallorum fossores*).
2. Goldsmiths (*inauratores*).
3. Surgeons administering mercurial inunction to syphilitics (*iatroliptae*).
4. Chemists (*chymici*).

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2. Franz Koelsch, in his book on Ramazzini (Stuttgart, 1912), lists these editions as follows: Latin: Modena, 1700; Utrecht, 1703, 1707; Venice, 1707; Leipzig, 1711; Padua, 1713; Venice, 1743; Padua, 1745. Italian translations: Venice, 1745; Milan, 1821; Venice, 1844; Naples, 1842. French: Paris, 1777, 1822 and 1841. German: Leipzig, 1705, 1718; Stendal, 1780, 1783; Ilmenau, 1823. English: London, 1705, 1725?, 1746, 1786. Dutch: London, 1724. A recent American version, very handy for seminary demonstrations, is that of Dr. Hermann Goodman, New York, 1933.

5. Potters (*figuli*).
6. Copper and tin-founders (*stannarii*).
7. Glass-blowers and mirror-makers (*vitriarii et specularii*).
8. Painters (*pictores*).
9. Sulphur workers (*sulfurarii*).
10. Blacksmiths (*fabri ferrarii*).
11. Plasterers (*gypsarii et calcarii*).
12. Apothecaries (*pharmacopaei*).
13. Scavengers (*foricarii*).
14. Fullers (*fullones*), all of whom suffer from respiratory affections due to dust and poisonous fumes, or to chemical poisoning.
15. Oil-men, tanners, butchers, fish-chandlers and cheese-mongers (*olearii, coriarii, casearii, fidicinarii*), and
16. Tobacconists (*tabacopaei*) who are apt to be pale, pursy, narrow-chested and sickly from the fetid atmosphere of their environment.
17. Grave-diggers (*vespillones*): malignant fevers, dyspnœa, dropsy, cachexia and sudden death.
18. Midwives (*obstetrices*): syphilis or other infections.
19. Wet-nurses (*nutrices*): phthisis; hysteria, skin eruptions, headache, vertigo, dyspnœa, diseases of breasts.
20. Vintners and brewers (*oenopaei et cerevisarii*): inebriety and alcoholism.
21. Bakers and millers (*pistores et molitores*): colds from meal-dust and overheating, horny hands and sometimes hernia.
22. Starch-makers (*amylopaei*): headaches and coughs.
23. Corn-sifters (*cribratores*): cough, dropsy, conjunctivitis and pruritus.
24. Stone-cutters, masons and brick-layers (*lapicidae*): dust (respiratory) diseases.
25. Washer-women (*lotrices*): menstrual disorders, dropsy and eczema.
26. Flax and oakum pickers and silk-spinners (*carminatores*): cough and conjunctivitis.
27. Bath-keepers (*balneatores*): skin and venereal diseases.
28. Salt-makers (*salinarii*): hunger, thirst, dropsy, ulcers and cachexia.
29. Those who work standing (*statarii*): varicose veins, crural ulcers, weak stomachs, stone and general debility.
30. Those who work sitting (*sedentarii*): stiff limbs and crooked backs.
31. Jews: diseases incident to rag-picking and other inferior occupations forced upon them in the Middle Ages.
32. Couriers (*cursores*): dyspnœa, pleurisy, hæmoptysis and emaciations.
33. Horsemen (*eqisones*): hernia, hæmorrhoids, boils and perineal ulcers.
34. Porters (*bajuli*): hernia, spinal deformities, varicose veins, pulmonary emphysema, hæmoptysis and phthisis.
35. Wrestlers (*athletae*): Wounds, apoplexy, laceration of blood-vessels, aneurysm and sudden death.
36. Those whose work strains the eyes (*lepturgi*): Disorders of vision.
37. Orators and singers (*phonasci et cantores*): laryngitis or even hernia.
38. Farmers (*agricolae*): mainly respiratory and digestive disorders.
39. Fishermen (*piscatores*): colds and fevers resulting from exposure.

the hygienic welfare of those who work with their hands. Observe that, at the very beginning of his book, he makes a fairly good classification of trade diseases:

"The various and numerous diseases, produced in artificers by the exercise of their respective trades, are, in my opinion, derived principally from two causes: first, the noxious quality of the matter on which they work, and which, by breathing out noxious steams, and subtile particles offensive to human nature, gives rise to particular diseases; and in the next place certain violent and disorderly motions, and improper postures of the body, by which the natural structure of the vital machine is so undermined as gradually to make way for violent distempers."

For two centuries after the appearance of Ramazzini's book, the subject of industrial medicine expanded steadily up to its present proportions. Up to the last quarter of the 19th century, this was accomplished mainly by special monographs, even as Ramazzini had built up his historic background out of isolated cases and observations.

Tissot and other 18th century physicians were much occupied with the hygiene and diseases of literary men, of men of the world, of people of fashion; but the real impetus came from industry. The list of occupations in Ramazzini's book implies a great expansion of workshops. Small factories originated in the 16th century and prior to 1801, there had been about 20 in Germany (Stieda). The modern expansion began in England with the spinning jenny (1767-71), the power loom (1785) and the application of steam to manufacturing industry. The population of Lancashire increased from 166,200 (1700) to 1,336,854 (1831), with a high toll of disease and death among this vast industrial proletariat. In these factory towns, the young were worn out before manhood; the average lease of life among industrials was 22 years, the death rate 36 per 1000. The workmen regarded themselves as "slaves" and their factories as "slaughter-houses." English labor legislation began with Sir Robert Peel (1801) and pyramided steadily up to the Workmen's Compensation Act of 1897, with its amendments (1900, 1906). France followed suit in 1810. Sir Humphrey Davy's safety lamp for coal-miners was invented in 1815. There followed such special monographs as those of Thackrah (brass founder's ague, 1832), Tanquerel des Planches (lead, 1839), Mélier (tobacco, 1849), Delpech (rubber, 1863), Hillairet (chromium, 1869-76), culminating in such large general treatises as those of Hirt (1871-8), Eulenburg (1876), Albrecht (1894-6), Weyl (1908), Oliver (Dangerous Trades, 1902), Goldmark (Industrial Fatigue, 1912), Thompson (1914), Kober (1916) and Alice Hamilton (Industrial Poisoning, 1925). Museums of Industrial Safety were established in Berlin (1904), Vienna (1908), New York (1911), and much has been accomplished by way of industrial insurance and compensation, industrial nursing, exhibits, pamphlets and posters.

Thus was launched a specialty which has some prospects of becoming, like book-keeping or theology, a perfect science, complete in all its parts and sufficient unto itself. The initial spade-work was done by Ramazzini 234 years ago. But our subject is susceptible of a larger and more comprehensive generalization; for it requires no greater amount of mental effort to perceive that every living creature, from the primordial cell to the highly civilized human being, is occupied, from birth to death, in being itself, in living its own life in its own way, and that from this conflict of so many separate existences comes most of the troubles and evils associated with life.

The word "disease" implies that the patient is ill at ease from some disturbance or alteration of the normal physiologic rhythmus of his life. In old English usage, this commonly meant lack of ease, without reference to pathological conditions. Thus a writer of 1450 says: "They shall have great disease for lack of water"; and Chaucer observes that to come down in the world is "a great disease" for the wealthy and prosperous. John Knox (1544) refers to a man "who would not disease himself to hear a sermon." Jeremy Taylor (1667) evidently envisaged conditions like the present when he preached that "The disemployed is a disease and like a long sleepless night to himself and a load to his country." Fuller (1661) speaks of "bad Latin" as "a catching disease" in a certain period. Time and again has this archaic usage engaged the fancy of poets:

"First lean thine aged back against mine arm,
And in that ease, I'll tell thee my disease." I King Henry VI, II, 5.
"A dedicated beggar to the air,
With his disease of all-shunn'd poverty." Timon of Athens, IV, 2.
"What racking cares disease a monarch's bed." Congreve, Mourning Bride.
"The strange disease of modern life." Matthew Arnold.

To the waspish wit of Pope, the idle-minded existence of spoiled ladies of fashion in the 18th century was the disease of people occupied in doing nothing:

"The fair one's feel such maladies as these,
When each new night-dress gives a new disease."

Elsewhere, he refers to "this long disease, my life," in other words, to the fretful existence of a captious, sensitive, high strung being, whose defensive reactions always took the pathway of biting wit and mordant satire. At this point, it is comparatively easy to generalize our equations and to visualize ourselves, or other people, as victims of the occupational disease of living out our particular lives as an adjustment of being to environment. Thus, the Scotch readiness to leap into argument is embalmed in the reputation of a certain Lord Advocate, that his whole life was a prolonged disputation; where a dunce was described as having spent a life of sixty years in "wondering what it was all about." So too, Carlyle saw the life of Rousseau as "a long soliloquy." Your convert to a particular creed is almost invariably a fanatic, where those bred in the faith or born to the purple are easy-going and tolerant. A pediatrist will have very little success in his practice if he does not see little people as particular cases of adjustment to environment, not always as easy to ticket off as adults. The most illuminating views which have been shed upon this matter come from such keen clinical observers as Charcot, Sir Jonathan Hutchinson, Osler and Clifford Allbutt. Charcot's teaching was to the effect that there is a classical stereotyped, base-line medicine, conveyed in the formal descriptions of disease-types in the textbooks; but each neurotic, rheumatic or arthritic patient is a problem in himself, and the symptoms of his disease may be distributed in space and time, between himself and his ascendants, descendants and immediate relatives. Or, as he put it in another way, "A nosographer is not necessarily a clinician." Morbid heredity or the real inwardness of the case might be concealed by the patient or his family, or he might be inarticulate, like the infant, or unable to give a clear statement of his condition through defect of education. It was up to the students to elicit the information. "Disease," said Charcot "is from of old and nothing about it has changed. It is we who change, as we learn to recognize what was formerly imperceptible." Or again, "The condition of the patient is only an accident in the history

of the disease, just as each of us is only an accident in the history of humanity." There are many strange diseases, thought to be modern, which have been vaguely outlined in the Hippocratic scriptures, although neither labelled nor recognized as such by their authors. Why then, Charcot inquires, did Hippocrates fail to recognize such a disease as pseudo-hypertrophic paralysis, which probably existed in his time? How did Duchenne come to discover it? Because a new set of facts is apt to baffle us and leave us cold, when "our minds have to take in something which deranges our original set of ideas; but we are all of us like that in this miserable world." To Charcot then, his neurotic, arthritic and rheumatic patients were accidental aspects, if not museum specimens, of diseases, the total symptoms of which were distributed in space and time and some phases of which, the particular patient was occupied in illustrating. As an accidental and partial illustration of the total history of the disease; it might seem, at first sight, as if the patient's contribution to the clinical picture were more important than himself. Nevertheless, each of Charcot's patients received careful clinical and humane consideration at the Salpêtrière, and the success of his clinic and practice (the largest in the world) was conditioned by the fact that most of the patients, streaming to him from all parts of the world, got relief of some sort, if not recovery. Allbutt's clinical approach was somewhat different. To him the patient was everything, the disease a convenient clinical summation in short hand, to check upon his condition and his chances of recovery. To Allbutt, such expressions as "a clinical entity," "a typical case," and suchlike, were anathema, allied to the primitive savage's notion of an indwelling disease-demon. The disease is not an entity but a peculiar alteration of the physiological make-up of Brown, Jones or Robinson, which we check by text-book descriptions. "There is no such thing," he said, "as typhoid fever, as angina pectoris, as spleno-medullary leukaemia, and so forth; the things so-called are Wilkinson, Johnson and Thompson, who, after their kinds, are afflicted not alike, but within such limits of similarity as to lead us to

class them together and to form a general conception of them. . . . If we are to speak of 'entities' of disease, these must not be the names, nor even our concepts, but the things, the thing Thompson and the thing Wilkinson in certain phases of their being. The moment we depart from these objects, we desert the names of things for the names of abstractions, in which no entity can lie. . . . Diseases are not even species, such as cats or toads, but abnormal, though not altogether irregular behaviors of animals and plants." We are now very close upon the trail of life as an occupational disease. For health itself, in Allbutt's view, is only a diathesis, or mode of growth and development, like scrofula or syphilis, and merely more popular among us as being more useful and serviceable to us in the long run. "The particular cycle which we call health we prefer as being the most useful variety of the human plant, as it is the most varied and complex; for this reason, we take it as a standard." The rest is merely the tyranny of words. Thus, a patient of gouty heredity is occupied with being gouty; in other words with the adjustment of his particular diathesis to environment, which may comprise exposure to dyspepsia, arthritis, phlebitis, arteritis, nephritis, neuritis, bronchitis and so on. A person with a predisposition to tubercle has to reckon with the possibility of becoming tubercular; a victim of the neurosyphilitic diathesis may be exposed to chorea, hysteria, insanity, migraine, eczema, angina pectoris, asthma, gastralgia and catarrhal symptoms; a member of a rheumatic family to purpura, urticaria, pemphigus, erythema, endocarditis, chorea and arthritis. These multiform aspects of basic diatheses Allbutt found to be distributed among the members of familial groups in Yorkshire. Hutchinson was one of the first to follow up the hæmorrhagic and ocular manifestations of gout, wrote on the pedigree of disease, and like Charcot, envisaged certain patients as "Mrs. T's legs" or "Mr. J's nose." Osler's viewpoint is summed up in his bedside aphorism: "Treat the patient rather than the disease." Like Allbutt, he studied the polymorphic aspects of an arthritic diathesis, pivoting around an erythema, a line of

thought which has been brilliantly elucidated latterly by Libman, with reference to the arthritic background, subacute bacterial endocarditis and the minute semeiology of pain. To appreciate this viewpoint, we have only to reflect that fever, pneumonia, epilepsy, paralysis and many skin affections were once regarded as full-fledged diseases, but are now merely symptomatic of something else. The major diatheses, like the major infections, are protean in semeiology.

The concept of disease as a physiological adjustment or occupation is, of course, susceptible of facile application to the group of endocrine disorders. It would seem almost trite to repeat the "endocrine catechism": Why are giants stupid? Why are dwarves malicious? Why are tall men inclined to be bullies? Why are great generals often small-sized men? Why do pimples go with petulance? Why are fat men gossips? When do maidens get moustaches? When are grown-ups infantile? Why do the aged of both sexes get to look alike? Whence the recent passion for slenderness?

The modern doctrine of the constitution, although old as the hills, has acquired some very significant data with reference to the schizophrenic and manic-depressive types. Predisposition to pernicious anæmia or peptic ulcers may be associated with a definite facies and physical habitus (Draper). The old mediæval doctrine of the four temperaments is based upon the ancient theory of the four humors and the belief in astrologic influences. The sanguine or Jovial man is blonde, chesty, ruddy, florid, expansive, cheerful—

> "Fit for all company and all fashion:
> Though bold, not apt to take offence, not ireful,
> But bountiful and kind and looking cheerful,
> Inclining to be fat and prone to laughter,
> Loves mirth, and music, cares not what comes after."

The choleric or Martial man, whose being was supposed to be permeated with yellow bile, is short, dark, thick-set, wide-chested, red faced, bold, touchy, combative and ambitious. The lymphatic, phlegmatic or Mercurial man is fat,

short, moist, easy going, lazy, good natured and indifferent. The melancholic, atrabilious or Saturnine man is thin in form, aquiline in feature, retiring, studious, pensive, suspicious and secretive. These four types have now been assimilated by Kretschmer to the three main categories of psychiatry. Jovial and Mercurial people are assimilated to the pycnic, cycloid or manic-depressive type, full-faced, full-bodied, of excellent digestive capacity, exposed to ups and downs of exhilaration and depression. Martial people assimilate to the athletic or muscular type; and Saturnine people come under the schizoid or praecox type, sharp-featured, thin bodied, thin-blooded, pale or sallow, with the split (schizoid) or shut-in personality of the Ishmaelite, at war with the world. Since Kretschmer's time, characterology has acquired many bizarre approaches, associated with the investigation of family records and the findings of dermatology, endocrinology, physical anthropology and ethnic psychology. We hear and read of the motor type (*Bewegungsmensch*) or man of action (*Leistungsmensch*), which is merely Kretschmer's athletic type over again; while his pycnics correspond to the "man of feeling" (*Gemütstypus*) and his schizoids to the asthenic, sensitive or mimosa type (*Empfindungstypus*). Psychic variants of these are the standfast, enduring peasant type (*Verharrungsmensch*), rooted in the soil and capable of going on forever; the actor type (*Darbietungsmensch*), who impersonates or dramatizes himself at the expense of other people; the redemptioner type (*Erlösungsmensch*), who is concerned to redeem or lift himself out of environmental disabilities; the mystic or desert type (*Offenbarungsmensch*), impelled by a mysterious call of divine revelation within; and the placid, self-exempting or seceding type (*Enthebungsmensch*), a cross between the pycnic and the schizoid. All these types have innumerable variants, effected by crossing and racial inmixture.[4] But most of

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4 For details, see the extensive literature of characterology of recent vintage, notably such books as L. F. Clauss: Rasse und Seele. 3. Aufl. München, 1933 or W. Böhle: Der Körperform als Spiegel der Seele, Leipzig & Berlin, 1929.

these categories are empirical, superficial, conceived from an arbitrary angle, and consequently of little positive value to the clinician.

The object of university education is to train the student to make use of his mind and do his own thinking. In the view of President Ames, the criterion of education (or civilization) is the dominance of reason over emotion in individual conduct and thought. At the bedside, this particular approach is essential and it is plain that the greater physicians were occupied in being physicians, in other words, in envisaging their patients, good or bad, as human problems, occupied, for the most part, in being themselves. A good doctor will tell you that it is impossible and futile to reason with unreasonable persons. Weir Mitchell, was sometimes so cantankerous over the caprices and intransigence of his neurotic patients that it transpired in his official correspondence. Osler referred to the grim visage in the Sargent portrait as his "Monday morning face." Charcot, through life-long association with neurotics and through his habit of mimicking their gaits and gestures in clinic for didactic purposes, came to acquire some of these tics and tremors himself. When he mimicked the propulsive gait in paralysis agitans, he seemed to be the patient. Toward the end of his life, he shuffled to his carriage with this queer gait, although not himself a victim of paralysis. Whether in the savage or civilized, human activity might be visualized humorously as a vast array of occupational neuroses. This is particularly true of the extravagances of the post-bellum period and accountable for its relative intellectual mediocrity. The transition from the stable, moribund social order, shattered by the World War, to a change of things, not as yet materialized, might be likened to the "Chaos" in Haydn's Creation. Nations, as well as individuals become fanatically self-determined and self-willed, bent upon the *salto mortale* of uncharted courses, ignoring the lessons of history and the experience of the past, committed to lines of thought and action likely to defeat their own object and so abut in nothing. The old Greek ideal of

aristocracy, as "the best that human nature is capable of," became confused with a sham autocracy or *vie de parade* of comedians and "bad actors," qualified mainly by almost complete lack of insight into human nature and human affairs. The gulf between the impersonal, reserved type and the sensational, exhibitionist type is the age-old difference between the liberal-minded, genial people, who have made gifts to humanity and the narrow, self-seeking, self-referential have-not. The reliable safeguard against to "wondering what it is all about" is the cool self-possession implicit in a "sense of humor"; in other words, that quick and ready perception of the laughable aspects of human adjustments to life, which alone makes society possible and human contacts endurable.

F. H. GARRISON.

HISTORICAL POINTS OF INTEREST ON THE MODE OF ACTION AND ILL EFFECTS OF MERCURY *

E. WILLIAM ABRAMOWITZ

INTRODUCTION

The recorded existence of mercury dates back to about 1600-1500 years B.C. According to Almkvist[1], this metal was shown to be present on analysis, in the tombs of the eighteenth or nineteenth dynasty of ancient Egypt. It is not known how the Egyptians obtained it, for what purpose they employed it, or even what they called it. It seemed certain, however, that they did not use it medicinally.

Neither the Bible nor the Talmud of the Hebrews, nor the Papyrus Ebers (1553-1550 B.C.), give us any clue as to the existence of mercury.

Ancient Greece knew of mercury four hundred years B.C., probably through contact with the Egyptians. The Greeks considered mercury poisonous and only made use of the metal in the arts and various industries. Hippocrates (460-357 B.C.) according to Dietrich[2], made no mention of mercury as a drug. During the time of Plato (429-347 B.C.), the physicians of Greece were prohibited under penalty of death, from prescribing mercury and other drugs of a poisonous nature. Aristotle (384-322 B.C.), Theophrastus (382?-287 B.C.), Pliny (23-79 A.D.), Dioscorides (40-54 A.D.), the compiler of the first materia medica, also Galen (131-201 A.D.), and even Aetius as late as the fifth century A.D., used mercury only to a limited extent as an external remedy. Alexander Von Tralles (525-605 A.D.) employed a cinnibar compound for various diseases and Paul of Aegina (625-690 A.D.) ordered mercury for certain intestinal disorders.

Medical historians have found little of value regarding mercury, in the works of the old Roman period, excepting what was copied from the Greeks.

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India probably had knowledge of mercury at the time of Buddha (500 B.C.). The physicians of old India were probably the originators of mercury as a healing agent and were sufficiently informed to know that severe gingivitis could follow its use. They employed it extensively, both internally and externally and knew the black, yellow, red and white forms of this drug. The medicinal value of mercury became known to the Persians through contact with India.

When the Arabs conquered Persia in 650 A.D. they learned of the therapeutic value and contributed a great deal of original observation on the medicinal and toxic action of mercury. They called the drug "Zaibach" or "Zaibar." Greek influence caused them to apply it only externally, for fear of its poisonous nature. In 857 A.D., Aben Mesue used charred mercury with oil and also with vegetable ingredients. He applied it in the form of rubs as a cleansing agent in various itchy skin diseases. Abugerig in 900 (?) A.D., knew of the toxic action of mercury vapors. Mirepsius was the first to mix metallic mercury with a fat. Rhases (860-932 A.D.) fed mercury experimentally to monkeys to determine its toxic action. He also tried various oxides of this metal therapeutically. The sublimate and the red precipitate of mercury became known. Avicenna, Albucasis and Serapion, also Arab physicians of this period, made other contributions on the external remedial value of mercury compounds. They employed it for conditions like pediculosis, the itch, impetigo, pustular affections, various swellings of the skin and leprosy (Almkvist).

The Chinese also possessed some knowledge of mercury. They called it Schui-jin which means liquid silver. Dietrich[2] cites a tale of a Chinese prince who died after taking an "elixir of life" containing mercury. This is said to have occurred about the year 745 A.D. The use of this drug is not mentioned again until about 1075, when it was applied in the form of rubs and inhalations, at first for parasitic skin diseases, and later on for syphilis. The Chinese knew of mercurial oxidation products and combinations of the element with sodium chloride, with salpeter, with sulphur and also with arsenic.

How Mercury Came to be Used in Syphilis

Medieval Europe entertained Greco-Roman ideas regarding mercury until further knowledge of this drug reached them through the Moorish invasion, the Crusades and the Latin translations of the Arabic by a monk, Constantinus Africanus (1087) and his colleague Nicolaus. It was advocated as an external remedy by Roger in Salerno as early as 1180. Toxic symptoms such as fetid breath, stomatitis, angina, intestinal and nervous manifestations had already been noted by the Arabs. The salivation encountered following its use was not attributed to the direct toxic action of this metal until Theodoric, Bishop of Cervia (1205-1298) and Guy de Chauliac (1300-1370) established their relationship. They thought it was of beneficial action. Thus the salivation cures were originated, using a series of rubs with some form of mercury ointment, principally for gouty afflictions. They recommended, however, the local use of honey in the mouth subsequent to a course of mercury rubs, to ameliorate the resultant disturbances that affected this area. In the thirteenth century, a common method of treatment for malum mortuum (leprosy), scabies, cancer and gout, was by means of a series of mercury rubs. These were continued until the patient developed either salivation or soreness of the gums. When syphilis became prevalent at the close of the fifteenth century, a similar course of procedure was followed. Jacob Berengario Carpi is usually credited as the originator of this form of antisyphilitic therapy. In "The Life of Benvenuto Cellini" the same Carpi is mentioned as being in Rome promising to work miracles in the "French disease" by means of certain fumigations. He undertook to give the cure only after receiving fees running into hundreds of crowns. Cellini states that Carpi would have been murdered if the latter had stayed any length of time in Rome, because most of those he had treated became considerably worse.

Differences of Opinion as to the Usefulness of Mercury in Syphilis

Differences of opinion as to the efficacy of this remedy against syphilis developed early. According to Sudhoff and Singer[3], various physicians like Schelling (1495), Gruenpeck (1496), Widman (1497), Gilino (1497) and Steber (1498), emphasized its value. Steber did not stress its use. Torella (1497) first employed it and then rejected it. Leonicenus (1497) rather discredited its specific action. Natale Montesauro (1498) was sceptical of mercury cures.

In the sixteenth century, mercury was commonly in use throughout Europe as an antisyphilitic agent, mainly in the form of rubs. Jacob Cataneus in 1504 resorted to the inhalation method. Johannes Benedictus and Johannes de Vigo advocated the mercury red precipitate pills. De Vigo, who later introduced the Neapolitan cream as a more efficient mercury ointment, also used a mercury plaster. Bichloride dressings were also advocated. These investigators, together with Angelus Bologninus and Nicola Massa, praised mercury as an excellent agent against the ravages of syphilis. Other physicians of this era took exception either to the drug or to the method in which it was
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tributed much to the ill repute that was heaped on this valuable remedy, at that time and later. Jerome Fracastor (Hieronymus Fracastorius, 1478-1553), who first used the term syphilis in his poems and scientific treatises, extolled the action of mercury as an anti-syphilitic remedy.

A vivid description of the mercurial treatment then in vogue for syphilis, is found in a book by Ulrich von Hutten (1519), entitled "De Guaiaci Medicine et Morbo Gallico." Von Hutten, a German Knight and not a physician, was afflicted with syphilis and had taken mercury cures for many years without benefit. He described[5] how the patients were shut up in a hot room and rubbed with mercury ointment for twenty to thirty days or more. The throat, palate, cheeks and tongue became infected and ulcerated, the gums swollen and the teeth loose. There was a profuse and continuous flow of saliva accompanied by an unbearable stench from the mouth. Because of this the patients were unable to eat or retain anything. Some developed vertigo and tremors, and even became insane. A few died in the room where they were being treated, from suffocation, from heat prostration or from anuria. In spite of the severity of the treatment, many of those who survived, developed syphilitic relapses later. Von Hutten extolled the virtue of guaiac for the treatment of syphilis and perhaps was somewhat biased on account of the poor results obtained by mercury in his own case, but it can be said that the mercurial treatment pursued was certainly a rigorous one and it was no surprise that some patients preferred to die of their disease, rather than submit to the cure. This led to the use of other drugs for the treatment of syphilis, and regimens like the "Entfettungskuren" of Hermann Boerhave (1668-1738), all based on various misconceptions of this disease prevalent at the time.

Ancient Conceptions on the Mode of Action of Mercury

It is of historical interest to follow the explanations given for the mode of action of mercury. The Greeks thought that mercury was effective because of its weight. Later when

syphilis appeared, Paracelsus (1493-1549) compared the action of mercury to the cold and the moon. He believed that mercury applied externally not only drove the temperature of the body inward, but the syphilitic process as well, and engendered a chronic constitutional disease through the combined action of the drug and the disease for which it was used. He therefore recommended the use of mercury internally (he favored turpeth mineral) to drive the noxious factors to the surface. Others reverted to the Galenical theories of medicine and explained the action of mercury as due to an uneven balance of the humors. Thus Thomas Sydenham (1624-1689) believed that syphilis could not be cured without salivation. Excepting in debilitated patients, he insisted on three ounces of mercury ointment (one ounce of the metal and two ounces of lard) to be rubbed for three successive nights and was only satisfied as to its efficacy, if the patient's output of saliva amounted to two quarts in twenty-four hours[6]. Jean Astruc in Montpellier (1684-1766) described a series of symptoms from the use of mercury in syphilis, and said these symptoms were due to the formation of excess waste products in the blood. To prevent them, it was necessary to bleed, purge, diet and salivate the patients. Van Swieten in Vienna and others, however, rebelled against the necessity of salivation cures in syphilis, but this idea was sidetracked by the celebrated John Hunter (1728-1793). The latter conceded that mercury was a truly specific remedy against syphilis, but believed that in the presence of syphilis or scrofula, the irritant action of the drug produced a constitutional disorder that merited to be considered as a separate entity.

Condemnation of the Use of Mercury

John Pearson[7] in 1800, one of the followers of John Hunter, labelled this constitutional disorder "Erethrismus mercurialis." Abernethy[8], another disciple of Hunter, spoke of it as "Pseudosyphilis"; still another, Andrew Mathias[9], called it "The mercurial disease."

The manifestations in the various organs and the skin of this so-called "mercurial disease" will not be described

here. The historical sequences that led up to it are mentioned in order to explain how the skin eruptions and systemic effects, like bone lesions, evidently brought on by syphilis were attributed to a combination of effects from mercury and syphilis, or to mercury alone, in a person of scrofulous dyscrasia. The "avirulists" like Francois Broussais (1772-1838), Jean Caron (1745-1824), and others in France even denied or doubted the existence of syphilis, except as a superficial disorder amenable to ordinary antiphlogistic remedies. In 1839, P. J. Murphy[10] of London, wrote that what was until then considered as the secondary symptoms of syphilis, was mostly due to mercurial effects. In Germany, Dietrich in 1837 disputed the teachings of John Hunter and Mathias, but nevertheless compared the effects of mercury to a gouty or rheumatic disposition and described thirty-eight different clinical manifestations of the disease, many of which he evidently confused with syphilis. A mercurophobia developed that finally reached its height in 1855 in the dictums of Joseph Hermann of Vienna, who stated that there was no such thing as secondary syphilis, but a chronic hydrargyrosis instead. He condemned the mercurial treatment of syphilis as a crime against humanity and stated that mercury was capable of producing in man, all the signs and symptoms of what was called secondary syphilis[11].

Clinical and pathological differences between syphilis and mercurial effects were difficult to portray even by Virchow who entered this violent controversy. The real coup de grâce to Hunter's hypothesis came with the experimental work of Overbeck in 1861, who showed there was no bone affection produced by mercury either in animals or man. Skin eruptions from the use of mercury in man could occur. Gastro-intestinal lesions, nephritis and other systemic diseases could also be produced by mercury both in man and animals, but much that was attributed to mercury was due to syphilis or other causes in no way connected with mercury. Kussmaul that same year came to the same conclusions. After that "mercurial disease" ceased to exist as an entity.

Mercurial Eruptions

Most investigators were so preoccupied with the action of mercury in syphilis, that recorded observations of mercurialism in those not affected with syphilis were entirely ignored or disputed. Bonetus in 1686 and Jussieu in 1719 are said to have noted some skin rashes in workers exposed to mercury. Jussieu mentioned a pustular eruption, parotid swelling, aphthae and salivation, in miners engaged in the extraction of the metal in Spain. The first definite reference however, is by Benjamin Bell[12] of Edinburgh, a contemporary of John Hunter, who contested the latter's views on the action of mercury and the existence of a constitutional mercurial affection. Bell in 1793 cited cases of syphilis that developed a morbilliform eruption following the use of various mercurial preparations. He observed others with urticarial and vesicular lesions. He was definitely convinced that these were due to the drug, irrespective of the preparation used or its mode of administration. He also noted the occurrence of pustular lesions, following the use of mercurial inunctions. John Pearson of London, claimed he had knowledge of such eruptions due to mercury as early as 1781 and had described them in his lectures in 1783 as "Mercurial Eczema." J. Gregory of Edinburgh, described such lesions as "Erythema mercuriale." A monograph by George Alley of Dublin appeared in 1804, entitled "An essay on a peculiar disease arising from the exhibition of mercury," followed by a more detailed publication in 1810 by the sa ne author on "Observations on the hydrargyria, or that esicular disease arising from the exhibition of mercury." A. Moriarty[13] also of Dublin, published his observations in 1804, on eruptions from mercury and at the suggestion of his teacher, Whitely Stokes, gave it the name of "The mercurial lepra."

Nomenclature of Mercurial Eruptions

About this time, the subject of mercurial eruptions attracted considerable attention not only in England but throughout the Continent. In addition to such terms as mercurial erythema, mercurial eczema, hydrargyria and

mercurial lepra, other observers added new ones, no doubt due to the variety of lesions observed following the use of this remedy. Thus J. Frank[14] in 1812 contributed "Exanthema mercuriale" and placed this eruption in a single category with the rashes of scarlet fever, measles, varicella, etc. G. Schmalz[15] in 1825 added the name of "Spilosis mercurialis" (mercurial spots). Devergie[16] in 1826 and Lagneau in 1828 wrote of "Erysipelas mercuriale" in their respective treatises on syphilis. Crawford[17] in 1820 preferred the term "Eczema rubrum" of Bateman, on account of the vesicular lesions encountered and also because he did not believe with the others that mercury was the only exciting cause. Biett, also Cullerier and Ratier[18] in 1833 and Cazenave in 1839 denied or doubted the existence of mercury eruptions. Dietrich[2], however, in his monograph (1837), described such skin lesions although he appeared to have confused some of them with syphilides. Others like Alexandre[19] in 1835, Ascherson [20] in 1837, Azum[21] in 1844 and Baron[22] in 1850, cited definite case reports of eruptions produced by external application and others by the internal administration of the drug.

In 1861 appeared the works of Overbeck[23] and Kussmaul[24] definitely establishing the existence of eruptions from the use of mercury. Kussmaul added a new designation "Dermatitis mercurialis" to the eight terms then extant, to describe the lesions on the skin produced by this drug. Auer[25] in 1860 reported a morbilliform eruption that followed the oral administration of small doses of the bichloride. Bazin[26] considered that such skin eruptions followed mostly after the external use of this remedy and that he had only seen two or three cases after its internal use during many years of an extensive practice. Nevertheless, reports continued to appear of such eruptions following oral administration. Ferrand[27] in 1868 reported a morbilliform erythema also following the inhalation of mercury.

Köbner's[28] article in 1877 was of especial importance inasmuch as he took the stand that only those eruptions should be considered as drug eruptions, that were produced by internal administration, subcutaneous use or through

EARLY 19th CENTURY DERMATOLOGY AND THE BROTHERS MAHON*

THEODORE ROSENTHAL

The dawn of the nineteenth century saw many revolutionary changes in medicine as well as in world affairs. Groups of earnest investigators and practitioners in every country of Europe, undisturbed by political upheaval and turmoil, could be found devoting their attention to the study of cutaneous diseases. In England there were Willan (1757-1812), Bateman (1778-1821), and Samuel Plumbe (about 1837); Joseph Plenck in Vienna (1732-1807), Peter Frank (1745-1821) and his gifted son Joseph Frank (1771-1842) in Germany; and that succession of notable figures in France, beginning with Lorry (1726-1823), Alibert (1768-1837), Biett (1781-1840), and a little later Cazenave (1802-1877), Rayer (1793-1867) and Bazin (1807-1878).

It was an age of intense scientific activity; Priestly and Lavoisier (1774-1777) had, in the closing years of the preceding century, identified the mysterious phlogiston as the element oxygen; Charles Bell (1774-1842) and Marshall Hall (1790-1857) were doing fundamental work in the physiology of the nervous system, while in the hospitals of Paris Pinel studied mental diseases, Orfila laid the foundations for the new science of toxicology and legal medicine, Dupuytren and Lisfranc did memorable work in surgery, Laennec introduced auscultation, and with Corvisart and Louis, studied problems in internal medicine; and Baudelocque accomplished his famous investigations in the field of obstetrics.

Contemporaneously with these, states Brodier, at the central admission office of the hospitals, the Mahon brothers, who were empirically healing the ringworm sufferers of Paris with their epilating salve, investigated the origin and nature of these affections and the younger brother gave the world the first description of tinea tonsurans.

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* Read before the Section of Historical and Cultural Medicine, May 9, 1934.

The specific cause of no disease was known, and the study of gross and microscopic pathology was yet to be undertaken. The medical men of the period were, perforce, compelled to content themselves with the physical characteristics of disease, and busied themselves chiefly with minute and exact description and classification of the morbid entities that they were able to recognize. Lack of classification, and imperfect classification, had seriously hampered the progress of the study of cutaneous diseases.

The high lights in the development of proper classification are briefly as follows: The first was introduced by Mercurialis (De Morb. Cut. 1576), adopted by Daniel Turner (1667-1741) (Tr. des. Mal. de la Peau 1743: English edition earlier) and again revised by Alibert in 1806. The basis of this classification is the seat of the disease, one group being for the head, and one for the rest of the body. Alibert called cutaneous affections of the head "teignes," and those of the body "dartres." He would then append the proper descriptive adjective, depending on whether the eruption was dry, moist, crusted, etc.

The next classification was that of Plenck (1790), which was subsequently improved upon by Willan. Plenck was the first to reject topographical differences, and to arrange cutaneous diseases according to their external characteristics. He committed the error however, of confusing the products of inflammation with the true anatomical characters of the disease. Willan's modification, which was a great step forward, was to reject all products of inflammation, and to divide the elementary lesions of the skin into eight orders.

The third classification was advanced by Joseph Frank, who, following the example of Noel Retz (1790) and Derien (1804), divided cutaneous diseases into acute and chronic ones. This seemed a natural division, but proved impracticable.

It was an age of unrest. Political revolution in France, and later the Napoleonic wars with their aftermath involving all of Europe, and the industrial revolution in Eng-

land, all contributed to the uncertainty and restlessness of the times.

The spirit of the French revolution however, did not interfere with the development and progress of science in France. Medicine, and Dermatology in particular, made great advances in the decades following it. On the 27th of November, 1801, the St. Louis Hospital was made a hospital for Skin Diseases. As a result, a tremendous impetus was given to the study of dermatology in France, and French dermatology reigned supreme for the first half of the century.

Possibly the one subject which gave rise to more controversy and dispute at the time, was that embraced by the general term of parasitic diseases. Generations of conjecture regarding the cause of scabies were put at rest when Renucci, in 1834, first demonstrated the *Acarus scabiei* at the Hôpital St. Louis. This had been preceded by the amusing deception practiced by Galès in 1812, whose organism proved to be the mite found in spoiled cheese. The modern knowledge of human ringworm infections dates from Schönlein's (1839) and Gruby's (1841) independent researches into the nature of favus.

The term Tinea, or Teignes, to denote ringworm infections, is an ancient one whose origin is shrouded in obscurity. According to Pusey, Cassius Felix first used the word Tinea about 400 A. D. in his summary of medicine, including skin diseases. Bazin states that the word is found first in the writings of Etienne of Antioch, who translated Arabian works, but that it had also been used popularly to indicate the tenacity and persistence of the disease it denotes. The great physicians of the Italian Renaissance, like Mercurialis, designated all diseases of the scalp as Teignes. The term was used in the middle ages by Guy de Chauliac, among others, who recognized five kinds of tinea (T. favosa, T. ficosa, T. amedosa, T. uberosa and T. lupinosa) and subsequently by Ambroise Paré who reduced the number to three species (T. ficosa, T. furfurosa, and T. corrosiva).

Alibert, who at the beginning of the 19th Century represented the old traditions in French medicine, adopted the classification of Teignes of Guy de Chauliac in his first works. Later, in changing it, he made a rather serious error. Up to this time, T. lupinosa designated our modern favus, and the term favus indicated our present day impetigo. Alibert abandoned T. lupinosa and called it Favus. This error was noted later by Gilbert and Feulard, and it was due to this error that our modern favus was given its name.

In England Willan and Bateman had classified the ancient French Teignes under the name Porrigo. To these authors, P. lupinosa remains the tinea vera of the ancients, and P. favosa is our impetigo. But this classification could not prevail in France over the error committed by Alibert. Hence it is by the name of Favus that the "vraie teigne" of the ancients, the tinea vera that was first recognized by medical men, is known today, not only in France, but also in England and throughout the entire world.

Biett, the first Willanist in France, and the former disciple of Alibert, changed the P. favosa of Willan from its original sense to designate the *vraie teigne*—Favus. The same word in the works of Bateman and Biett, therefore, indicates two different entities. Biett, in addition, abandoned the other Willanistic porrigos. He had confused P. scutulata, our *teigne tondante* (ringworm of the scalp), and combined it with favus, a serious error which necessitated a new discovery of something which had already been described. Bateman had also studied as a separate disease, what he called P. decalvans, the alopecia areata of the entire world. Biett did not support this doctrine of Willan; hence *la pelade* (alopecia areata) remained confused with the scars of favus, under the term Favus sine Favis (Alibert), a mistake which further complicated the situation. In short, Biett, again in accordance with tradition, ended by keeping the term Porrigo for the Favus. In the same way Rayer, who frequently drew on the preceding century (the 18th) for inspiration, returned to the conception of the single tinea, and from now on it was called only Favus.

Favus was not the only contagious parasitic disease of the scalp. There is a group of others designated today as Tinea tonsurans (*Teignes tondantes*), ringworm of the scalp. The history of these has been far more involved than that of Favus. The former nearly always presented a uniform picture, whereas ringworm of the scalp differed greatly in clinical appearance, and also frequently appeared on other parts of the body.

English medicine, since the 16th Century, had recognized under the name ringworm, the lesions which were later called in France herpès circiné and teigne tondante. Bateman, who recognized that it was contagious and epidemic termed it Herpes Circinnatus. Samuel Plumbe, in his "Practical Treatise of Diseases of the Skin" (London, 1824) also recognized that the scalp affection might produce lesions on other parts of the skin. He also was the first, incidentally, to suggest epilation for tinea tonsurans.

Willan and Bateman had classified ringworm of the scalp with the Porrigos. They distinguished six types: P. lupinosa, our Favus, and under P. scutulata, they described ringworm of the scalp, giving rather a mediocre description. The other Porrigos were P. larvalis, impetiginous eczema; P. furfurans, our pityriasis capitis; P. decalvans, our alopecia areata; and P. favosa, impetigo contagiosa.

These authorities had even less success in the treatment of these vexatious infections than they had with their proper classification and nomenclature. The fate of the child with ringworm of the scalp a century ago was indeed a sorry one. The only methods of treatment extant were most cruel and inhuman. A favorite was the calotte, which is a leather disk smeared with pitch and then applied to the scalp. When removed with a brisk twitch, the adherent hairs are uprooted *en masse*. Other methods involved the use of irritating ointments and solutions, which occasionally gave rise to severe constitutional reactions, and, more rarely, to fatal sequelae. Treatment consumed months and even years.

It is most interesting therefore, to learn that at this time, the Administration of Hospitals of France had entrusted the treatment of these affections to the two brothers Mahon, laymen, who evidently, to judge from the report below, were able to secure superior therapeutic results.

The following is an extract of a report made to the General Welfare Council in 1816, by one of its members, on the state of the hospitals and asylums in Paris, from January 1, 1804, to January 1, 1814.

"The treatment of ringworm at the central admission office of the hospitals in Paris was instituted by decree on the 31st of December, 1806, and a similar treatment commenced at the Infants Hospital.

'Before adopting the remedy of the Mahon brothers the Council had conducted a two year trial of it at the St. Louis Hospital, under the eyes of its own physicians; their report was favorable. From 1809-1813 it was tried on 795 children; 527 of these were cured. 196 were not cured, or, if they seemed to be, the disease recurred, and 72 were still under treatment on December 31, 1813. The Mahon brothers received in addition to a yearly stipend of 1000 francs each, six francs per capita for the children declared cured.' "

This then, was the confused condition and uncertain status of parasitic diseases in the first decades of the nineteenth century in France, when, in 1829, there appeared a handsome octavo volume entitled "Récherches sur le siège at la nature des Teignes" by M. Mahon the younger, one of two brothers, who, though laymen, were officially entrusted with the treatment of these diseases in the hospitals of Paris, Lyons, Rouen, Dieppe, Elbeuf and Louviers.

This book, consisting of a lengthy 40 page introduction, 373 pages of text, and five excellent colored plates drawn by M. Zwuinger, son-in-law of the elder Mahon, represents a significant milestone in our knowledge of these diseases. It was the first volume entirely devoted to such a specialized subiect and considers thoroughly all aspects of the question

in approved monographic style. The date, 1829, is noteworthy, as being before the discovery of the specific agents causing these infections.

The foreword is a quotation from Alibert (Précis theorique et pratique sur les maladies de la peau) indicating the desirability of more careful and exact researches into the origin of Teignes, or parasitic diseases of the scalp.

The preface contains a lengthy declaration of gratitude to the Administration of Hospitals of Paris for deigning to entrust the treatment of tineas to the Mahons, thereby providing them with the means of making thousands of observations of all types of this disease. They wish to thank, among others, Alibert, Richerand, and Biett, for assistance in their work.

In the introduction, the words of Alibert are quoted to show the incentive for undertaking the work. The diligence of the studies, and as a result, the ability to separate off into other groups diseases which formerly were classified with the tineas is alluded to.

The classification followed by the Mahons is: T. faveuse, T. tondante, T. amiantacée, T. furfuracée, T. muqueuse, T. granulée, Crasse laiteuse, Crasse membraneuse. A chapter is devoted to each species. Chapters on differential diagnosis and treatment, with tables showing the results of successful treatment conclude the book.

Mahon the elder, according to Sabouraud, discovered ringworm of the scalp and named it. His description seems to be of the type recognized today as Microsporosis, and was far more complete and explicit than that of Willan and Bateman. It described various sized areas denuded of hair, with broken off hairs visible; in these areas the skin is bluish, and when scratched, covered with whitish dust. Not only is it described thoroughly, but mention is made of its frequent transmission to the glabrous skin and to the finger nails. Both trichophytosis and favus of the nails are described and identified as two separate entities, Mahon emphasizing the thickening and distortion of the nail, and

the difference in color, being white in the former condition, and yellow in favus. Thus the most important manifestations of the disease were simultaneously and precisely recorded by an observer who was not even a physician.

As a matter of interest, Favus of the nails was discovered by one of the Mahon brothers, who accidentally infected himself while epilating a patient with his finger nails. He was thus enabled to observe the course and evolution of the disease at first hand.

The chapter on treatment is very wordy, replete with apologies and mentions all the treatments that have been employed except their own. Several histories of fatal accidents ensuing after treatment are reported. As to their own treatment, they merely state that it is simple, requires hospitalization, and that large numbers of patients can be treated by a few men. They even compute the cost of treatment per day as 1.25 fr. per patient.

They state that a great day would dawn if they were able to divulge their secret, but because of sacred family duties, and inviolable stipulations they cannot reveal the nature of their treatment.

This, of course, was merely a necessary expedient because of the financial consideration involved. If they were to make public their methods, their only means of livelihood would soon disappear. Suffice it to say however, that the Mahons had, very early in their experience, realized the importance and usefulness of epilation; they used their finger nails and became expert in their use. Epilation with forceps had thus fallen into disuse after Guy de Chauliac, Paré, Astruc and Sauvage. The mysterious ointments and secret powders used by the Mahons were undoubtedly employed to put the inquisitive off the track.

The original work and discoveries of the brothers Mahon had surprisingly little reverberation. It is true that Alibert, in his "Monograph sur les Dermatoses" (1832-1835), alludes to tinea tonsurans, and several of his pupils named it, but there is evident confusion of terms and ideas. At the

same time, Alibert, as physician to the St. Louis Hospital, surely was very well acquainted with the work of the Mahons. The majority of contemporary writers ignored absolutely tinea of the scalp, neither mentioning it nor describing it. Brocque and Hardy in recent historical sketches of the work in the St. Louis Hospital, make no mention of the Mahons. Léon Meunier, in his history of medicine, contains no reference to them. However Rayer, in his second English edition, states, "Of all the depilatory methods proposed, that of the Messrs. Mahon is unquestionably the best. They begin by cutting the hair, etc., removing incrustations with flour poultices . . . then the parts are annointed with the depilatory ointment; later an epilatory powder is used, in conjunction with a fine comb." A few pages later, Rayer again mentions the work of the Mahons and also quotes from a report of the analysis of their proprietary remedies published by M. Bracconot. Three powders were employed, and their chemical constitution proved to be essentially an impure subcarbonate of potash.

Gruby, in his report on the organism subsequently named *Trichophyton endothrix*, mentions Mahon in the title of his paper.

Thomas Bateman, in his 8th edition of "A Practical Synopsis of Cut. Dis. according to Dr. Willan," mentions Mahon's method of removing infected hairs in Favus (p. 216). He also mentions Mahon in his bibliography.

Bazin, in his "Affections Cutanées Parasitaires," 1862, cites Mahon repeatedly and in a complimentary fashion (p. 152). After stating that the younger Mahon deserves the honor of being the first to name and describe the entity of tinea tonsurans, he cannot understand upon what basis are founded the reproaches which Alibert and later Cazenave, directed toward him.

In 1840 Cazenave re-discovered tinea tonsurans and gave a masterly clinical description of it, and made the first differentiation of ringworm of the scalp from alopecia areata. It seems entirely probable that the diagnosis of

ringworm of the scalp in France from 1830-1840 was made only by the brothers Mahon, laymen.

An intensive search for bibliographical data relating to these interesting brothers has been most disappointing. Medical periodicals, both contemporary and modern, have, as was to be expected, completely ignored them. Even at the Hôpital St. Louis, where they worked for years, there is no information available as to their lives. Prof. Léon Brodier, the distinguished historian, has assured me that he is unaware of any document bearing on the brothers Mahon, considered, to use his own words, "as charlatans by French dermatologists." The publishers J. B. Baillière et fils, the same firm that brought out the Mahons' book over a century ago, also have no knowledge whatever of any facts concerning the Mahons.

Quérard, in *La France littéraire* (Vol. 5), mentions the younger Mahon, in connection with the book, and gives his date of death as October, 1833, at Paris. This apparently conflicts with other data supplied by Brodier, who stated that Mahon jeune wrote another book in 1868, published also by Baillière, entitled "Considerations sur le traitment des Teignes" which is listed incorrectly in the Index Catalogue under the name of Mignot-Mahon. I have been unable to obtain a copy of this book. In this volume, again quoting from Brodier, he stated that he had a son and two sons-in-law, called Vaconin and Mignot-Mahon, who also busied themselves with the treatment of la teigne. There was also a son-in-law of the elder Mahon, named Guilbert.

The brothers Mahon, and their family, conducted for many years a private clinic in Paris, devoted to the treatment of ringworm infections, which was situated at the Rue du Pas-de-la-Mule. The clinic was maintained by their descendants until 1914. One of the best known of these, Paul de Molènes-Mahon, who died in 1916, published a thesis on Polymorphous Erythema in 1884.

The spectacle of a non-medical family attaining to special skill and ability in the diagnosis and treatment of a particular disease is not unusual in the history of medicine, and

not limited to dermatology. An outstanding example is that of the famous Thomas family of bonesetters of Liverpool, who flourished at about the same time.

Sabouraud, who evinces a most friendly spirit to the Mahons, calls them "empiriques," empiricists, or possibly lay healers. This term is surely less opprobrious than charlatan, employed by Brodier. Col. Garrison, in his recent delightful paper on Quackery, undertakes to describe three types of medical imposters; speaking of the charlatan, he describes him as "the Doctor Know-all of Grimm's fairy tales, whose top-heavy assumption of omniscience ranges anywhere from parade of erudition to maundering about the ultimate nature of disease." Not so with the Mahons; it is safe to say that had they possessed the necessary professional qualifications, their book would have been hailed as a solid contribution to dermatology, indeed a landmark of progress. It is true that by keeping their methods and remedies secret, they violated the fundamental canons of medical ethics, but not being of the profession, they should be judged by more charitable and elastic standards.

More than a century has gone by, and it does not seem proper that the name of these brothers who, working during an entire generation, accepted by their illustrious contemporaries, officially certified by the government in their special capacities, and securing genuine therapeutic successes in a field where all others had encountered failure, should be relegated to oblivion.

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RESOLUTION PASSED AT THE OCTOBER MEETING OF THE COUNCIL RE: GRADUATE FORTNIGHT OF 1934

The Council of the Academy has noted with great satisfaction the splendid success which attended the Graduate Fortnight for 1934. The Council has been informed by the Director that this success resulted from the enthusiasm with which the Committee on Medical Education, the Sub-Committee on the Fortnight, the Committee on Exhibit, and the members of the Academy staff worked to provide a most interesting program and exhibit. Therefore,

BE IT RESOLVED, that the Council formally express its appreciation of the work done and extend a vote of thanks to all those, including the exhibitors and the associated hospitals who took part in this gratifying accomplishment. The Council directs that this action be published in the Academy Bulletin.

J. MARION SIMS, M.D., LL.D.
1813-1883

REDEDICATION OF THE MEMORIAL TO J. MARION SIMS

OCTOBER 20TH, 1934

A few months ago, Dr. I. Seth Hirsch informed the Academy authorities that in a Park Department storage yard he had seen the statue of J. Marion Sims, which had been removed from Bryant Park. The President and Director communicated promptly with Commissioner Robert Moses, and as promptly were assured that he would gladly meet our wishes, and would arrange to have the statue placed in a niche of the wall of Central Park, at 103rd Street and Fifth Avenue, facing the buildings of the Academy of Medicine and the Museum of the City of New York.

The Park Department did even more. The statue was thoroughly overhauled and was placed on a new and beautifully designed pedestal. There it now stands, revealing for all time, in a convincing pose, Doctor J. Marion Sims, as physician, scientist and thinker.

The medical profession and the community owe especial thanks to the Honorable Robert Moses, Commissioner of Parks, and his able assistants, Messrs. Andrews and Fields.

REDEDICATION EXERCISES

Dr. Bernard Sachs, President of The New York Academy of Medicine, said:

On behalf of The New York Academy of Medicine, and the medical profession of the city and of the country, let me express the great satisfaction that we feel that the memorial of Dr. J. Marion Sims has been placed in full view of the building of the Academy and of the Museum of the City of New York.

New York has every reason to perpetuate the memory of a man who was great not only as a surgeon but as also one of the illustrious citizens of his day. Happy we are to rededicate this statue to Dr. J. Marion Sims, of whom my old friend, Dr. Paul F. Mundé said at the first unveiling—

> "Among the many great eminent physicians and surgeons which America has produced, he stands pre-eminent as the man through whose genius a mere branch of medical science and practice was so elevated as to create an era in medicine and raise America from the place of pupil to the proud position of teacher of older nations."

To-day we look upon J. Marion Sims as the founder of modern gynecology; as the pioneer among American abdominal surgeons.

No one did more than did Dr. Sims in the second half of the last century, to give American surgery its present authoritative position among the nations of the world.

I recall from my own student days in the late seventies in the various universities of Europe, that as an American citizen, I was proud to hear Sims extolled everywhere as the exponent of American surgery.

While we shall always be ready to do honor to the name of Dr. J. Marion Sims as physician and gynecologist, he deserves to be especially lauded as one of New York's eminent citizens, and to do justice to this phase of his career, we shall now listen to Dr. John H. Finley.

Dr. Finley said:

Dr. Sachs, Mr. Commissioner, Ladies and Gentlemen:

It is a great honor to be appointed (for I was not elected, except in the theological sense) to speak for the citizens of New York in rededicating this monument. The ceremony is significant in that it gives evidence that the city, through its Park Department and Municipal Art Commission, is to cherish and guard with greater care its memorials of those whom it promised to remember.

To an ancient Roman, Cato, who was called "the Censor," is imputed the saying, "I had rather it should be asked why I had not a statue than why I had one." Many a person to whom a statue has been erected would rather not have had one than see it neglected or marred. I am myself especially grateful not only that this statue has now been given a fit setting but also that Washington Irving, who has stood lonesomely in Bryant Park on a shabby pedestal, is now to

have assurance, thanks to the Park Department, that he is still dear to this city. My next concern is for Horace Greeley, that he may have more suitable placement than his monument, half hidden by the elevated station, now has.

By the side of the most beautiful street in all Britain (Princes Street in Edinburgh) and in the company of the statues of Scotland's illustrious sons, poet, preacher, statesman, soldier stands a monument to a great doctor—James Young Simpson. His service to humanity was akin to that of Dr. Sims of America, whose brilliant achievements, as the original epitaph relates, "carried the fame of American surgery throughout the civilized world." The family of Dr. Simpson declined a grave for him in Westminster Abbey, but his friends erected a monument to him in that fair street in the heart of Scotland. So our American doctor, who would have been eligible had he been an Englishman, for a little space in her Abbey, has now been given a permanent place beside our "Via Gloriosa"—Fifth Avenue—a street which

> In glory surpasses all the rest—
> The Main Street of the Empire of the West,
> Where all the nations of the earth
> Have set their gifts of greatest skill and worth;
> A path of glory that leads not to the grave
> But is, as that fair street of golden pave,
> An endless avenue of hope and praise
> The "via gloriosa" of all ways.

For years I have seen the crowds pass to and fro in Forty-second Street as heedless of this monument which stood for years on the edge of desolation as if it were only granite and bronze without name or nation. Now it not only has the kindliest environment that nature can give for residence in this great city, but also the continuing recognition by his profession of Dr. Sims's contribution to the science of human healing, standing as it now does on this famed street, between the Academy of Medicine and the Museum of the City of New York and between two of our great hospitals. Here may it remain as long as Medicine keeps here its greatest Academy.

If there were room for an added epitaph, I would suggest the line from Homer in which praise is given to the doctor. In simplest translation into English, it would read: "The physician is worth a host of us."

Dr. George Gray Ward, Chief Surgeon of Woman's Hospital, said:

Mr. Chairman, Ladies and Gentlemen:

James Marion Sims was of English and Scotch-Irish descent. He was born in South Carolina in 1813, graduated at Jefferson Medical College in Philadelphia in 1835, and practiced in Montgomery, Alabama, where he did general surgery until 1854, and died in New York in 1883.

Gynecology is the science of diseases and injuries peculiar to women. For centuries little was known and less done to alleviate the sufferings women had to endure until gynecology developed into a special field of medical study in the middle of the 19th Century.

Sims from the Southland came to New York in 1854 and proclaimed to the medical world that he had discovered and perfected a method whereby it was possible to cure a hitherto incurable condition, the result of injury during childbirth.

In those days, owing to the lack of obstetric knowledge and care, every community had in its midst women suffering excruciatingly from an injury that practically excluded them from society at large. The efforts of surgeons throughout the world to repair this injury had hitherto failed, therefore, when Marion Sims demonstrated that he had succeeded, the greatest interest was aroused, as now there was hope for these pitiful outcasts.

Sims tried for four years before he succeeded in curing his first case. His patients were negro slaves, and he operated forty times on three patients, and twenty-one times on one of them during his experimental work, and remember this was before the days of anaesthesia and aseptic surgery.

His success was due to his discovery of the principle involved necessary to obtain an adequate exposure of the injury and for which he devised an instrument, and the employment of silver wire stitches which did not become infected and thus allowed the wound to heal.

Sims came to New York in 1854 and demonstrated his operation, and the result of his efforts was the founding in 1855 of the Woman's Hospital in New York, which has the distinction of being the first hospital in the world to be established for the treatment of diseases peculiar to women.

From this beginning developed the study and discovery of methods of treatment of the various injuries that result from childbirth, of non-malignant and cancerous tumors, and of the infections that women are subject to, so that today Marion Sims is acknowledged as the Father of Modern Gynecology and the Woman's Hospital as its birthplace.

It has been said that his discoveries advanced the knowledge of diseases of women to an extent which could not have been done for a hundred years or more without his methods. Sims demonstrated his operations in many countries in Europe and one of his patients was the Empress Eugenie, wife of Napoleon III.

While circumstances led Sims to devote his life work to a specialty, his vision embraced the entire field of surgery, and he was foremost to advocate the prompt opening of the abdominal cavity for gunshot wounds of the abdomen.

The first Woman's Hospital, presided over by Sims, was located at Madison Avenue and 29th Street, the second on the block bounded by Park and Lexington Avenues and 49th and 50th Streets, on land which was donated by the city, and opened in 1867. The present hospital is situated at 110th Street, opposite the Cathedral of St. John the Divine, and was opened in 1906.

Professor T. Gaillard Thomas, of the College of Physicians and Surgeons, in an address to the graduating class of Cornell University Medical College, stated that in his opinion Sims was to be ranked with William Jenner, the

discoverer of vaccination for smallpox, as one of the men of all time who had done most for their fellow creatures.

Immediately after his death a movement for the erection of a statue in his memory was inaugurated in Europe and his native country. This was a spontaneous gift from his brothers in the profession throughout the civilized world, and from many of the unfortunate beings his genius and skill had benefited. South Carolina, his native state, has erected a beautiful memorial to him in Columbia.

The inscription on the old pedestal of this monument we are dedicating today tells the story of his career:—

J. MARION SIMS, M.D., LL.D.
Born in South Carolina, 1813, died in New York City in 1883.
Surgeon and Philanthropist.
Founder of the Woman's Hospital of the State of New York.
His brilliant Achievements carried the fame of American
Surgery throughout the civilized world,
In recognition of his services in the cause of science
and mankind
He received the highest honors in the gift of his
countrymen
And decorations from the governments of France, Portugal,
Spain, Belgium, and Italy.

And on the reverse:—

Presented to the City of New York
By
His professional friends, loving patients
And
Many Admirers
Throughout the World.

To Sims belongs the honor of arousing the profession and the laity to the needs of suffering women of his day, and by his genius and skill he made possible the cure of the numerous diseases and injuries that are peculiar to the sex, so that for all coming time he will have an enduring monument of his talent, his genius, and his philanthropy in the gratitude of woman, and in this statue of bronze a recognition of his having developed the great specialty of Gynecology as a result of the founding of the Woman's Hospital, which has contributed inestimable blessings to suffering womankind and to the advancement of medical progress.

RECENT ACCESSIONS TO THE LIBRARY

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Phil., Lippincott, [1934], 985 p.

Frahm, F. W. The principles and technics of full denture construction.
Brooklyn, Dental Items of Interest Pub. Co., [1934], 590 p.

Fraser, F. R. The principles of therapeutics.
Balt., Williams, 1934, 135 p.

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München, Bergmann, 1934, 359 p.

Kenyon, J. H. Healthy babies are happy babies.
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London, Milford, 1934, 274 p.
Legge, (Sir) T. M. Industrial maladies.
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Malzberg, B. Mortality among patients with mental disease.
Utica, State Hospitals Press, 1934, 234 p.
Martin, F. H. Fifty years of medicine and surgery.
Chic., Surgical Pub. Co., 1934, 449 p.
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N. Y., Macmillan, 1934, 533 p.
Mellanby, E. Nutrition and disease.
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N. Y., Macmillan, 1934, 248 p.
Mohr, O. L. Heredity and disease.
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Newburgh, L. H. & Mackinnon, F. The practice of dietetics.
N. Y., Macmillan, 1934, 264 p.
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N. Y., Macmillan, 1934, 658 p.
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St. Louis, Mosby & Co., 1934, 420 p.
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N. Y., Crowell, [1934], 529 p.
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N. Y., Macmillan, 1934, 454 p.
Williams, J. F. Personal hygiene applied. 5. ed.
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PROCEEDINGS OF ACADEMY MEETINGS

NOVEMBER

STATED MEETINGS

November 8

I. Executive Session—a. Reading of the Minutes; b. Election of Members; c. Election of Honorary Fellows; d. Report of Nominating Committee.

II. Paper of the Evening—The problem of acute appendicitis in New York City, Shepard Krech; Discussion: a. From the medical standpoint, William W. Herrick, b. From the surgical standpoint, John A. Hartwell; c. From the public health standpoint, Thomas Parran, Jr., State Commissioner of Health.

THE HARVEY SOCIETY (in affiliation with the new york academy of medicine)
November 15

The Second Harvey Lecture, "The Significance of the Amino Acids in Nutrition," William Cumming Rose, Professor of Biochemistry, University of Illinois.

SECTION MEETINGS

section of surgery—November 2

The Section decided to forego its November meeting in favor of the Graduate Fortnight. The program of the Graduate Fortnight for Friday evening, November 2, was arranged by courtesy of the Section.

section of dermatology and syphilology—November 7

I. Presentation of cases from University and Bellevue Hospital Medical College.

II. Discussion of selected cases.

III. Executive Session—Examination of cases is limited to members and their invited guests.

section of pediatrics—November 8—Public Health Meeting

I. Papers of the Evening—a. Public health problems and the pediatrist, John L. Rice, Commissioner of Health; b. Newer viewpoints regarding quarantine of communicable disease, William H. Park, Director of Laboratories, Discussion by Louis C. Schroeder, Hugh Chaplin, Haven Emerson, Samuel Karelitz, Roger Dennett, Camille Kereszturi, Harry Bakwin.

combined meeting of section of neurology and psychiatry and the new york neurological society—November 13

I. Psychiatry and the criminal law—a The psychiatric aspect, Bernard Glueck (30 minutes); b. The legal aspect, Prof. Jerome Michael (30 minutes)

II. Discussion—The Hon. Judge Cornelius F Collins, Foster Kennedy, James G. Wallace, Esq., J. Ramsay Hunt, Robert H Elder, Esq., Israel Strauss. General discussion.

section of historical and cultural medicine—November 14

I. Reading of the Minutes

II. Papers of the Evening—symposium on the atlas of the woodcuts of vesalius to be published by the academy, a The prospective atlas How it was begun and what it is to contain, Archibald Malloch; b The title pages of the *"De Corporis Humani Fabrica"* of Vesalius, Samuel W Lambert; c An historical query, Mr. William M. Ivins, Jr., Metropolitan Museum of Art (by invitation).

III. General Discussion—To be opened by Harvey Cushing, Yale University Medical School.

SECTION OF ORTHOPEDIC SURGERY—Notice

The meeting scheduled for November 16, 1934, was held in Philadelphia, where the members of the section were the guests of the Philadelphia Orthopedic Club. A program was arranged for the afternoon, starting at 2:15 p.m., and was followed by a dinner at 7 p.m.

SECTION OF OPHTHALMOLOGY—November 19

I. INSTRUCTION HOUR, 7 to 8 p.m.—Diagnosis of muscle anomalies, James W. White, John Dunnington.

II. DEMONSTRATION HOUR, 7:30 to 8:30 p.m.—a. Case examinations; b. Slit lamp studies, Milton Berliner, Isadore Goldstein, Wendell L. Hughes, Girolamo Bonaccolto (by invitation).

III. SECTION MEETING, 8:30 to 10:30 p.m.—a. Reading of the minutes; b. Case reports, 1. A case of silver oxide deposits in the cornea, James W. Smith; c. A desperate case of sympathetic ophthalmia, Arnold Knapp; Clinical history, O. P. Perkins; Pathological examination, B. F. Payne (by invitation); d. Scientific papers, 1. On the present methods of operating for detachment of the retina in Europe, Arnold Knapp; Discussion, John M. Wheeler, Mark Schoenberg; 2. Transient fluctuations in the scotoma of glaucoma, John N. Evans; Discussion, Ralph Lloyd, Conrad Berens.

SECTION OF MEDICINE—November 20

I. READING OF THE MINUTES

II. PRESENTATION OF CASES—a. A case of Graves' disease, Ephrain Shorr (by invitation); b. A case of chronic intermittent fever, David Seegal (by invitation); c. A case of chronic auricular flutter, Arthur C. DeGraff.

III. PAPERS OF THE EVENING—a. Creatin metabolism in Graves' disease, Ephrain Schorr (by invitation).

IV. GENERAL DISCUSSION—H. B. Richardson, Franklin M. Hanger (by invitation), John Wyckoff.

SECTION OF GENITO-URINARY SURGERY—November 21

I. READING OF THE MINUTES

II. PRESENTATION OF CASE—Anuria due to bilateral metastatic obstruction of the ureters, Stanley R. Woodruff, William Antopol.

III. PAPER OF THE EVENING—Practical applications of recent contributions to physiology of the upper urinary tract, William P. Herbst, Washington, D. C. (by invitation); Discussion to be opened by Edwin Beer, Robert Gutierrez.

IV. GENERAL DISCUSSION

V. EXECUTIVE SESSION

SECTION OF OTOLARYNGOLOGY—November 21

I. READING OF THE MINUTES

II. PAPERS OF THE EVENING—SYMPOSIUM ON UPPER RESPIRATORY INFECTIONS AND SOME OF THEIR COMPLICATIONS—a. The relationship between diseases of the ear and of the upper respiratory tract, James G. Dwyer; Discussion, John R. Page, Edmund P. Fowler; b. Upper respiratory infections from the pediatric standpoint, Louis C. Schroeder; Discussion, J. D. Craig, Samuel Karelitz; c. Endoscopy in the treatment of diseases of the upper respiratory tract, John D. Kernan; Discussion, David H. Jones.

SECTION OF OBSTETRICS AND GYNECOLOGY—November 27

Program arranged by the Staff of the Mt. Sinai Hospital

I. Three cases of endometriosis (adenomyosis) with special reference to etiology, Isidor C. Rubin.

II. Lymphogranuloma inguinale. Report of two cases, Morris A Goldberger, Jacob Auslander (by invitation).

III. Case management of urinary incontinence in women, Max D. Mayer

IV. An unusual ovarian tumor containing an oestrogenic hormone, Frank Spielman (by invitation).

V. The value of lumbar tympany in the differential diagnosis of large ovarian cysts, U. J. Salmon (by invitation).

VI. Ovarian carcinomata simulating acute surgical conditions of the abdomen, Phineas Bernstein (by invitation).

AFFILIATED SOCIETIES

NEW YORK ROENTGEN SOCIETY *in affiliation with* THE NEW YORK ACADEMY OF MEDICINE—November 19

I. PRESENTATION OF INTERESTING CASES.

II. PAPER OF THE EVENING—Primary carcinoma of the lung, B. M Fried.

III. DISCUSSION—Leopold Jaches, Ross Golden, Coleman Rabin.

SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE—NEW YORK MEETING—November 21

I Influence of intermedin on growth of mouse melanoma, K Sugiura

II. Pregnancy cells in rat pituitary: Influence of lipoidal corpus luteum extract, H A. Charipper.

III. Tissue culture studies on relation of sarcoma to leukosis of chickens, J Furth, E. L. Stubbs.

IV. Study of etiology of influenza, A. R. Dochez, K. C. Mills, Y. Kneeland, Jr

V. Active immunization of children against poliomyelitis with formalin inactivated virus suspension, M. Brodie.

VI. Shwartzman phenomenon with *B. pertussis* culture filtrates, L H Koplik (introduced by G. Shwartzman).

VII. Potentials in embryo rat heart muscle cultures, B M Hogg, C M Goss, K S Cole (introduced by H B Williams).

VIII. Note on metabolism of copper in splenectomized rabbits, M Sandberg, O M Holly.

IX. Physical basis for use of helium as a new therapeutic gas, A L Barach

JOINT MEETING—NEW YORK PATHOLOGICAL SOCIETY AND SECTION OF SURGERY—November 22

SYMPOSIUM ON NON-MALIGNANT TUMORS OF BONE—1 Pathologic aspects, Francis Carter Wood; 2. Roentgenological aspects, Raymond W Lewis, 3 Clinical and therapeutic aspects, Bradley L. Coley.

MEMBERS ELECTED NOVEMBER 8, 1934

Walter Gerard Hanlon. ....812 Park Avenue
Harold William Dargeon..............................1095 Park Avenue
Margaret McAllister Janeway ....140 East 54 Street
Harry Rosenwasser ....49 East 96 Street
William Henry Holzapfel.........................277 West End Avenue
Angelo M. Sala......................................1107 Park Avenue
Francis M. Conway...................................30 East 40 Street
James W. Toumey, Jr.................................525 Park Avenue
Edgar Mayer ....111 East 56 Street
Halford Hallock ....410 East 57 Street
Girolamo Bonaccolto ....106 East 60 Street
Eugene Bernstein ....100 Central Park South
L. Farmer Loeb......................................200 West 70 Street
Anne Topper ....320 West 89 Street
Siegfried Elias Katz ....722 West 168 Street
William J. Fordrung ....Scarsdale, N. Y.
Edward Ross Marshall............................Room 21, Barge Office
William H. Turnley.. ....322 Main St., Stamford
John Cohen ....1801 Weeks Avenue
Morris Greenberg ....168 West 86 Street
Richard J. Kelly....................................140 East 54 Street
L. Leonard Rothschild...............................116 West 59 Street
Leon Lantzounis ....133 East 58 Street
Robert Burlingham ....860 Park Avenue
Braham H. Golden ....10 East 90 Street
Robert J. Lowrie ....105 East 53 Street
Murray A. Last ....1123 Park Avenue
Alfred L. Malabre.......................452 Fort Washington Avenue
Jerome A. Marks.....................................145 West 58 Street
Herbert F. Traut ....111 East 60 Street
William L. Estes, Jr.........E. P. Wilbur Trust Co. Bldg., Bethlehem, Pa.

OBITUARY:

CORNELIUS GODFREY COAKLEY, 1862-1934

Dr. Cornelius Godfrey Coakley was born in Brooklyn, August 14, 1862, eldest son of George W. Coakley, Professor of Mathematics and Astronomy at New York University, and Isabelle Hoe Coakley. He received the degree of Bachelor of Arts from the College of the City of New York in 1884 and of Master of Arts in 1887. The degree of Doctor of Medicine was conferred upon him by New York University Medical College in 1887 when he graduated with first honors. He served as an interne in Bellevue Hospital and early began his distinguished teaching career as instructor in Histology and Anatomy in the school from which he graduated. Diseases of the Ear, Nose and Throat proved especially interesting to him, partly because, at that time comparatively little was known of them. After study and research here and considerable work abroad, being chiefly impressed by the work of Professor Killian, he brought back the best of the knowledge acquirable in Europe. In 1896 he became Clinical Professor and in 1905 Professor of Laryngology at University and Bellevue Medical College where he remained until 1914 when he accepted the chair of Otolaryngology at the College of Physicians and Surgeons of Columbia University.

His interest and ability in teaching and the clinical training of his students, internes and assistants never abated, and although inclined to be conservative, he kept abreast of any advances. His keen memory and long experience sometimes prompted him to say of innovations, that they had been tried and found wanting thirty or more years ago, before the present proposer knew anything of the subject.

Associated with the late Dr. Caldwell, he made valuable experiments and the first useful radiographs of the nasal accessory sinuses.

Dr. Coakley's amazing energy and well directed effort enabled him to accomplish much hospital work. He organized and founded the Ear, Nose and Throat Service at Bellevue Hospital in 1916 where he continued as Director until he was asked to establish a similar service at Presbyterian Hospital on the opening of the Columbia Medical Center in 1928. Since then he has assiduously worked to improve the service to patients having ailments of the ear, nose and throat, establishing a ward in the Babies Hospital a year ago. He was consultant to numerous other hospitals, including Bellevue, Woman's, Neurological Institute, Sloane Hospital, Southampton, Stuyvesant Square and Seaview Hospitals.

Among the professional societies he belonged to were The New York Academy of Medicine since 1894, Medical Society of the County of New York, New York State Medical Society, American Medical Association, American Laryngological Society, American Otological Society, American College of Surgeons, American Rhinological, Laryngological and Otological Society, the Société de Laryngologie des Hôpitaux de Paris of which he was elected a member after a series of lectures in Paris in 1924.

He was author of many articles in the field of his endeavor and a textbook used widely in many medical schools, "A Manual of Diseases of the Nose and Throat," the seventh revision of which was published in 1930.

Dr. Coakley's ability as a teacher is best exemplified by the outstanding careers of the many men trained by him, now scattered throughout the country.

His brilliance in his special field has been widely appreciated, not only in this country but in Europe and Japan. However, the memory that his host of patients, associates and friends chiefly hold of him is of his kindness, his helpful understanding of their difficulties and his unswerving integrity. Well may we say "There was a man."

James W. Babcock.

DEATHS OF FELLOWS OF THE ACADEMY

Fisher, Edward Dix, B.A., M.D., 30 East 40 Street, New York City; graduated in medicine from New York University in 1878; elected a Fellow of the Academy April 1, 1886; died November 23, 1934. Dr. Fisher was a member of the County and State Medical Societies, the American Neurological Association, the New York Neurological Society, the Society of Alumni of Bellevue Hospital and a Fellow of the American Medical Association. He was Emeritus Professor of Neurology at New York University and Bellevue Hospital Medical College, a former President of the American Neurological Association and of the Medical Society of the County of New York. Dr. Fisher had also been President of the New York Neurological Society, a Vice-President of The New York Academy of Medicine and Consultant to Bellevue, Willard Parker and St. Vincent's Hospitals.

Grausman, Philip M., M.D., 130 West 58 Street, New York City; graduated in medicine from the College of Physicians and Surgeons in 1900; elected a Fellow of the Academy October 7, 1909; died November 21, 1934. Dr. Grausman was a member of the County and State Medical Societies, a Fellow of the American Medical Association and of the American College of Surgeons. He was Chief Surgeon to the Hospital for Joint Diseases, Surgeon to Gouverneur and Lebanon Hospitals and Consulting Surgeon to Beth Israel Hospital in Newark. At one time he was Assistant Professor of Surgery at the New York Polyclinic Medical School and Hospital.

Smith, Harmon, B.A., M.D., 150 East 62 Street, New York City; graduated in medicine from Bellevue Hospital Medical College in 1897; elected a Fellow of the Academy November 7, 1901; died December 11, 1934. Dr. Smith was a member of the County and State Medical Societies and of the American Laryngological, Rhinological and Otological Society of which he was once a vice-president. He was a Fellow of the American College of Surgeons and of the American Medical Association. For some years he was professor of laryngology at Cornell University Medical College. At the time of his death he was a director in the throat department of the Manhattan Eye, Ear and Throat Hospital, consulting laryngologist to the Memorial and Babies Hospitals and consulting aurist to the Monmouth Memorial Hospital, Long Branch.

Smith, Theobald, M.D., Sc.D., Princeton, New Jersey, graduated in medicine from Albany Medical College in 1883; elected an Honorary Fellow of the Academy November 18, 1926; died December 10, 1934. Dr. Smith was Scientific Director of the Rockefeller Institute since its foundation in 1901, Vice-President of the Board from 1924 to 1933, at which time he succeeded Dr. William H. Welch as President. He was Director of the Department of Animal Pathology and a member of the Institute from 1914 to 1929. Many contributions of the first importance to medical science are attributed to him.

His research into the spread of the Texas cattle fever was the first proof ever given that insects are the essential intermediate agencies in the spread of some infectious diseases.

Many scientific bodies throughout the world have recognized his attainments and contributions. He received honorary degrees from Harvard, University of Chicago, University of Breslau, Washington, Princeton, Yale, Royal Hungarian Veterinary Academy, Budapest; Pennsylvania, Rutgers University of Giessen and University of Edinburgh.

He received many awards and medals from universities and societies in this country and abroad and was a member of outstanding medical and other scientific groups in this country, England, Scotland, Ireland, France, Denmark, Italy and Sweden.

STURMDORF, ARNOLD, M.D., 160 Central Park South, New York City; graduated in medicine from the College of Physicians and Surgeons in 1886; elected a Fellow of the Academy March 7, 1901; died November 13, 1934. Dr. Sturmdorf was a member of the County and State Medical Societies and a Fellow of the American Medical Association and the American College of Physicians. Dr. Sturmdorf also had been a professor at the New York Polyclinic Medical School and Hospital, Associate Surgeon to Woman's Hospital, Consultant to the Jewish Memorial, Community and Beth-El Hospitals, Chairman of the Section of Obstetrics and Gynecology of The New York Academy of Medicine, President of the New York Physicians Association and the Manhattan Medical Society. He was the author of a number of books and monographs on surgical subjects.

URQUHART, HOWARD DONALD, M.D., 115 East 61 Street, New York City; graduated in medicine from New York University in 1906; elected a Fellow of the Academy November 4, 1920; died November 8, 1934. Dr. Urquhart was a Fellow of the American Medical Association and a member of the County and State Medical Societies and the Society of Alumni of Bellevue Hospital. He was Orthopedic Surgeon to the Seaside Hospital and Associate Orthopedic Surgeon to the Polyclinic Hospital.

INDEX, 1934

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troglodyte experience was often like that ridiculed in the English witticism about fox-hunting: "the unspeakable in pursuit of the uneatable." In some such way, dietetics became the basic element in ancient therapy. In the Hippocratic tract on Ancient Medicine (430-420 B.C.), human concern about diet is associated with the dim and dubious origins of rational medicine itself. To the primitive Greek (say of Hesiod's time), poisonous plants and animals were already matters of avoidance (taboo). Wheat, barley, fruit, wine and olive oil were the main vegetable staples. Meat was more extensively consumed in the Homeric period than later; fish little, if at all. From his own uncomfortable sensations, the Greek rustic learned, by long experience of trial and error, to prefer cooked food to raw; to restrict diet to an irreducible minimum during acute illness; to ease the sick stomach with slop diet; to defer eating until the subsidence of a fever; to strike a sensible balance between gluttony and abstinence. Farmers and day laborers, used to one, at most, two meals a day, found themselves yawning, sleepy and stupified after the novelty of a mid-day meal; with the common experience of flatulence, colic and diarrhœa, if a dinner followed the lunch. In the hands of peripatetic physicians, such rude initial data became the starting point of a rational semeiology and dietetic therapy, as expounded in the classic utterance of Celsus: "In this way, medicine arose from the experience of the recovery of some, the death of others, differentiating the harmful from the salutary things." The inference that rational medical practice originated in some such way has a high degree of probability; in other words, gastro-enterology is probably the oldest phase of internal medicine, dissociated, at the start, from supernatural (speculative) causes. That the primitive harvest hands made good experimental animals is reflected in the verse of Horace:

> "Edit cicutis allium nocentius,
> O dura messorum ilia." (Epode III, 3-4)

In early Greek pathology, the very efforts of the body to bring the humors from a raw, fermented status (*apepsia*) to normal (*pepsis*) were associated with the idea of cookery

or coction, a view of digestive processes which survived until the 17th century. In the archæological remains of ancient Egypt, concern about food is already that of a well advanced civilization. We see the harvesting and marketing of fruit and grain; grape-arbors and fish-ponds; the kneading of dough; the brewing of beer; dining at table and the symbolic suckling of an infant at the udders of the cow Hathor. The Ebers Papyrus features intestinal parasites and the liver complaints common to all tropical and subtropical areas. In Assyro-Babylonian medicine, divination by inspection of the liver became an equivalent of prognosis. In the primer of Assyrian clinical medicine, which R. C. Thompson has pieced together from broken baked-clay tablets (1926)[2], there is already a respectable array of findings on diseases of the mouth alone. As assembled in the scholarly summary of Theodor Puschmann[3], the practical knowledge of digestive disorders, scattered through the literary remains of Greek medicine, was not inconsiderable. True, the clinical reasoning is clogged and obfuscated by the unbridled indulgence of the Greek physicians in speculating about the variable aspects of causation, by the general ignorance of human post-mortem appearances, by regrettable lack of the definite terminology necessary to classification, and by a pathetic groping toward clean-cut semeiology and therapy. Nevertheless, some of these clinical pictures of digestive disorders, embedded in the redundant expositions of Hippocrates, Celsus, Aretaeus, Galen and the Byzantine compilers, will be found to square with modern notions better than most.

The œsophagus, to begin with, while so denominated in Hippocrates, came to be envisaged as "the mouth of the stomach," the *cardia* of pre-Galenic writers. In Galen's time and thereafter, it was known as *stomachus*, both by the laity and the profession. By parity of reasoning, precordial distress (*morbus cardiacus*), while allocated to the heart by Erasistratus, Asclepiades and Aretaeus (*syncope*), was thought to be of gastric (eventually œsophageal) origin by Galen, Aetius and Alexander of Tralles. Caelius Aurelianus even differentiated a cardiac variety and a gastric variety, but the semeiology

2. Thompson: Assyrian Medical Texts. London 1926 (Englished in: *Proc. Roy Soc. Med.* (*Sect. Hist. Med.*), Lond., 1923-4, XVII, 1: 1925-6, XIX, 29.
3. Th. Puschmann: *Alexander von Tralles*, Wien, 1878, I, 204-259.